Medical Library

OCT 1 , 1930

VOLUME 40 NUMBER 4

AMERICAN JOURNAL

OF

DISEASES OF CHILDREN

EDITORIAL BOARD

CLIFFORD G. GRULEE, Chicago

OSCAR M. SCHLOSS, New York
FRITZ B. TALBOT, Boston
H. F. HELMHOLZ, Rochester, Minn.
W. McKIM MARRIOTT, St. Louis
L. R. DaBUYS, New Orleans
JOHN C. GITTINGS, Philadelphia

OCTOBER, 1930

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, January 4, 1911, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized on June 14, 1918.

CONTENTS OF PREVIOUS NUMBER

SEPTEMBER, 1930, NUMBER 3

Metabolism Studies in Nephrosis with Special Reference to the Relationship of Protein Intake to Nitrogen Retention, Edema and Albuminuria. D. Murray Cowie, M.D.; Katharine M. Jarvis, Ph.D.; and Moses Cooperstock, M.D.; with the Technical Assistance of Asa Nakao, M.D., Ann Arbor, Mich.

Heliotherapy and the Peripheral Blood. Gerald Hoeffel, M.D., and Dorothy Lyons, A.B., Boston.

The Diagnostic Value of Sodium Fluorescein in Epidemic Cerebrospinal Meningitis. Barnet E. Bonar, M.D., Salt Lake City, and Lyle G. Bailey, M.D., Millwood, Wash.

Acute Suppurative Thyroiditis in Children: Operative Recovery. J. M. Mora, M.D., Chicago.

A New Infant Feeding Chart. R. Wallace Teed, M.D., Owosso, Mich.

Differential White Count in Infancy: Comparison by Supravital and Fixed Smear Methods. Carl H. Smith, M.D., New York.

Sepsis with Leukopenia (Agranulocytosis) in Children: Report of Ten Cases. John A. Bigler, M.D., and Joseph Brennemann, M.D., Chicago.

The Preparation of Dextrose for Parenteral Injection. Francis F. Schwentker, M.D., Baltimore.

The Problem of Dental Caries. R. W. Bunting, D.D.S.; Faith Palmerlee Hadley, M.S.; Philip Jay, M.S., D.D.S., and Dorothy G. Hard, D.D.S., Ann Arbor, Mich.

Diffusible Blood Serum Calcium in Normal New-Born Infants. Hartsell Harrison Ray, M.D., and Nilkanth M. Phatak, B.S., San Francisco.

Pneumonia in Children: A Bacteriologic Study. Norman Plummer, M.D.; Antoinette Reis, M.D., and Selma Shultz, A.B., New York.

Nitrite Reaction as a Diagnostic Test in Influenzal Meningitis. Roy M. Greenthal, M.D., Milwaukee.

Case Reports:

Congenital Atresia of the Bile Ducts. A. Matheson, M.D., and I. Harrison Tumpeer, M.D., Chicago.

Infectious Mononucleosis. J. P. Price, M.D., Florence, S. C.

Gonorrheal Rhinitis. Ralph T. Miller, M.D., Boston.

Progress in Pediatrics:

The Psychiatric Aspects of Enuresis. Forrest N. Anderson, M.D., Los Angeles.

Pediatric Biographies:

William Heberden, The Elder. John Ruhrah, M.D., Baltimore.

News and Comment.

Abstracts from Current Literature.

Society Transactions:
American Pediatric Society.
Philadelphia Pediatric Society.

Book Reviews.

Directory of Pediatric Societies.

COPYRIGHT, 1930, BY THE AMERICAN MEDICAL ASSOCIATION

American Journal of Diseases of Children

VOLUME 40 OCTOBER, 1930 NUMBER 4

THE ALKALOSIS OF VOMITING AND THE ACIDOSIS OF ADVANCED RENAL DISEASE*

L. G. H. DRAKE, M.D., (Chief)

P. MARSH, B.A.

AND

J. L. GAMBLE, M.D.

BOSTON

From these and a great many Expressions to the same Purpose, in that Book of Hippocrates, it is evident that that most sagacious of Physicians established it as a Maxim that these second Qualities viz. Acidity, Bitterness, Saltness and the like, conjoined with the Symptoms of Cold or Heat are chiefly to be considered as the principal and efficient Causes of Diseases. And hence, I think, I need not scruple to add that it naturally follows, that the Cure of Diseases does not so much consist in extinguishing any increased degree of heat by a cold regimen as in blunting the Acidity, elaborating the Bitterness, or mitigating the too great Saltness of the Humors, as also in attenuating such as are thick, compacting such as are too thin and fluid, correcting the acrid and resolving the obstructed. *Harris: Upon the Acute Diseases of Infants, 1742.*

Our purpose in this paper is to present data descriptive of individual instances of disturbance of body fluid reaction and of the extent of repair obtained by the therapeutic measures used. The present knowledge of the pathogenesis of acidosis, of alkalosis and of the usually associated condition, dehydration, may be regarded as fairly satisfactory in that it provides one with easily legible indications for the treatment in these conditions by procedures that are simple and practicable. Undoubtedly, however, further study will greatly improve the conceptions regarding causative circumstances and one's appraisement of reparative agents. An obvious desideratum at present is a better understanding of the optimal intensity and duration of the application of the therapeutic measures at hand. These ends, it is believed, will best be gained by quantitative studies of individual clinical situations.

Owing to the number of interdependent factors that together establish the reaction of the blood plasma, measurements of them are best presented graphically. By this method the changes in the inorganic structure of the blood plasma that explain reduction or extension of the bicarbonate concentration are brought clearly into view. These relationships are not easily discernible in a tabular statement of the data. In this paper we have used the plan of diagram devised by Ross, Tisdall,

* Submitted for publication, April 17, 1930.

From the Department of Pediatrics, Harvard Medical School, and the Medical Division of the Children's Hospital.

and one of us (J. L. G.) [1] (chart 1). The diagram is constructed from measurements of the concentrations of the individual factors. The cations are superimposed in the left-hand, and the anions in the right-hand, column. The diagram indicates correctly that the skeleton of the plasma is composed, not of salts, but of individually sustained concentrations of

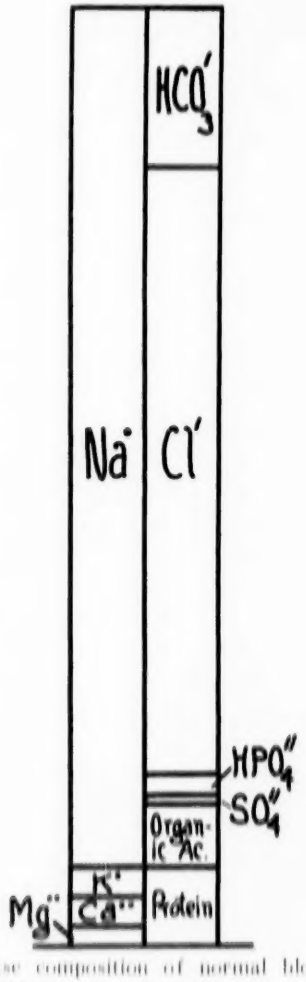


Chart 1.—The acid-base composition of normal blood plasma showing the relative values of the individual factors in terms of concentration. The bases are superimposed in the left-hand and the acid radicals in the right-hand column.

ions, and that the sum of the concentrations of anions is exactly equivalent to the sum of the concentrations of cations. Maintenance of this equivalence is obtained by the unique adjustability of the concentration

1. Gamble, J. L.; Ross, S. G., and Tisdall, F. F.: J. Biol. Chem. **57**:633, 1923.

of bicarbonate ions (HCO'_3) in the diagram. That is, change in any other factor or factors in this ionic structure will be compensated for by increase or decrease of HCO'_3 to the extent required to sustain the acid (anion) column in the diagram at exactly the same height as the base (cation) column. The acid-base equivalence in terms of concentration thus maintained does not, however, imply a constancy of blood plasma reaction. An increase of HCO'_3 above its usual value will cause a shift of reaction in the direction of alkalinity (alkalosis), and a decrease a shift in the opposite direction (acidosis). Changes in plasma factors that cause compensating alterations of bicarbonate will thus produce either alkalosis or acidosis of some degree.[2] Explanation of an abnormal bicarbonate concentration, therefore, must consist in finding the underlying changes in plasma structure. If one constructs a diagram from measurements of plasma factors obtained from a patient exhibiting acidosis or alkalosis and compare it with a diagram representing normal values, these underlying changes and their relationship to reduction or extension of the plasma bicarbonate can be brought into view. This is our purpose in the diagrams presented in this paper. They will be read easily if it is borne in mind that the bicarbonate concentration (HCO'_3) is determined by the extent to which fixed base is not covered by the sum of the concentrations of the other acid radicals.

In the study of clinical situations it is not practicable to measure individually all of the factors represented in chart 1. Such an undertaking would require an exorbitant sample of blood plasma. With the methods at hand, however, one can obtain measurements of total fixed base and of the two chief acid factors, chloride ion and bicarbonate ion, from a satisfactorily small sample. These data usually provide a nearly complete description of plasma changes accounting for a change in reaction. The diagrams to be presented are constructed from these three

2. This adjustability of the concentration of bicarbonate results from the fact that the other anions in the plasma are the radicals of stronger acids than carbonic acid and will dispossess bicarbonate ion of base to the extent that the sum of their concentrations rises above its usual value. If, on the other hand, recession of these radicals occurs, the fixed base thus uncovered forms bicarbonate by combining with "free" carbonic acid which is always at hand, and the bicarbonate concentration is thus extended. The reaction of the blood plasma is determined by the ratio of the concentration of this free carbonic acid (H_2CO_3), to that of bound bicarbonate ion, the HCO'_3 represented in the diagram. The concentration of free carbonic acid in the plasma is regulated by the rate and volume of lung ventilation; in the presence of change in bicarbonate, the respiratory mechanism undertakes adjustment of the free carbonic acid concentration in a direction which tends to restore the normal ratio of the two factors. This attempt at compensation from the point of view of preventing a change in reaction is, however, never more than partially successful. It is clinically visible as slow and shallow breathing in the presence of alkalosis and as somewhat rapid and, especially, deep breathing (hyperpnea) when the situation is one of acidosis.

measurements: total fixed base ($B^{\bullet}$), chloride ion (Cl') and bicarbonate ion (HCO'_3); the last factor, being adjustable, is appropriately placed at the top of the acid column. The remainder of base not covered by bicarbonate ion and chloride ion represents the base equivalence of the sum of the unmeasured acid factors; this value is designated (R') in the diagrams. In the instances when ketosis is a factor, the concentration of ketone acids found in the plasma is placed in the acid column and designated (K'). The actual concentration values, expressed as cubic centimeters of tenth-normal acid or base per hundred cubic centimeters of plasma, are also given in the diagrams. For further explanation and illustration of this method of study, the reader is referred to a paper by one of us (J. L. G.).[3] It should be mentioned here that Hartmann,[4] in his extensive studies of the changes in plasma structure produced by disease, used a perhaps more convenient type of diagram consisting of a single column which measures total base and on which are laid off the factors of acid equivalence. We preferred, however, to use the double column diagram because, in our opinion, it permits an easier reading of relationships.

MICRO-ANALYTIC METHODS

Total fixed base was determined by Fiske's method[5] and bicarbonate by that of Van Slyke.[6] The chloride measurement was obtained by an unpublished modification by Fiske of the Volhard procedure. For determinations of ketone acids the method of Van Slyke[7] was used.

THE ALKALOSIS OF VOMITING

The alkalosis of vomiting is a readily understandable event. Vomiting causes a continued loss of gastric secretions and thereby brings about a progressive withdrawal from the blood plasma of the water and substances used in the construction of these secretions. The substances thus taken from the plasma are chiefly sodium and chloride ion. The loss of chloride ion in secretions vomited from the stomach is usually several times as large as the loss of sodium. In consequence, there develops in the blood plasma and interstitial body fluids a much larger deficit of chloride ion than of sodium. This discrepancy is covered by an increase of bicarbonate ion. The alkalosis of vomiting thus consists simply in an automatic extension of bicarbonate ion replacing the excess of chloride ion over sodium lost in the vomitus.

---

3. Gamble, J. L.: New England J. Med. **199**:1318, 1928.

4. Hartmann, A. F.: Chemical Changes Occurring in the Body as a Result of Certain Diseases, Am. J. Dis. Child. **35**:557 (April) 1928.

5. Fiske, C. H.: J. Biol. Chem. **51**:55, 1922.

6. Van Slyke, D. D.: J. Biol. Chem. **30**:347, 1917.

7. Van Slyke, D. D.: J. Biol. Chem. **32**:455, 1917.

From the point of view of therapy it is essential to remember that continued vomiting of gastric secretions produces progressive dehydration, and that it is far more important to repair dehydration than to correct reaction. Most fortunately, however, the treatment for dehydration is also the treatment for alkalosis. The therapeutic measures indicated are extremely simple, namely, the administration of solutions of sodium chloride and of dextrose. The essential requirement is that, in the presence of severe dehydration, these agents be employed to a quantitatively adequate extent. Physiologic solution of sodium chloride serves to rebuild body fluid volume and also to correct defects in the ionic structure of the body fluids. As regards its adequacy in the latter respect, it is important to remember that it depends on an alert functioning of the kidney. That is, when salt solution is given abundantly, it is the kidney which, by controlling separately the excretion of sodium and of chloride ion according to their respective deficits within the body, reestablishes the normal values for the concentrations of fixed base and chloride ion and thus restores bicarbonate.[8] The fact that severe dehydration causes impairment of renal function is, therefore, of significance from the point of view of therapy. The essential factor seems to be simply a lack of available water. Provision of surplus water with the purpose of restoring renal function is thus indicated. The salt solution given tends to be retained because it contains the substances which rebuild body fluid volume. Dextrose solution, however, since it does not contain these "structural" substances, should excellently serve the purpose of bringing the kidney into active and accurate operation. We are indebted to Hartmann[4] for appreciation of the importance of the renal factor in disturbances of body fluid reaction accompanying dehydration. His extensive studies have thoroughly illustrated the various and severe distortions of plasma structure resulting from failure of control of concentrations by the kidney. And there are other services which dextrose provides. If given intravenously as a 10 per cent solution, it greatly hastens the absorption and distribution of subcutaneously delivered salt solution. Also it will remove an accumulation of ketone acids if this circumstance is present. And, by its protein-sparing effect, it should greatly reduce the consumption of body protoplasm due to the factor of starvation which is present in situations causing continued vomiting. These several considerations support the use of dextrose solutions as an important accessory agent in the treatment for dehydration. For a more comprehensive discussion of dehydration accompanying severe disturbances of gastro-intestinal function and of the indicated therapeutic measures, the reader is referred to a recent paper by one of us (J. L. G.).[8]

8. Gamble, J. L., and Ross, S. G.: J. Clin. Investigation **1**:403, 1925.

CASE 1.—*Duodenal Obstruction.*—A girl, aged 11 years, following an attack of abdominal pain, vomited food and fluids for seven days before entering the hospital. She was extensively dehydrated. Breathing was somewhat slow and noticeably shallow. A qualitative test for ketone acids in the urine was strongly positive, but sugar was not present. She did not complain of pain, but continued to vomit when given food or fluids. Examination of the abdomen by palpation produced no information. The finding, however, of a huge reduction of plasma chloride gave important support to the presumptive diagnosis of obstruction.

The acid-base composition of the blood plasma at entrance is shown in diagram 1 of chart 2. By comparing this with the "normal" diagram, several abnormalities are easily evident: an extensive loss of chloride ion (Cl'), an increase of bicarbonate ion (HCO'_3), the presence of a large concentration of ketone acids (K')

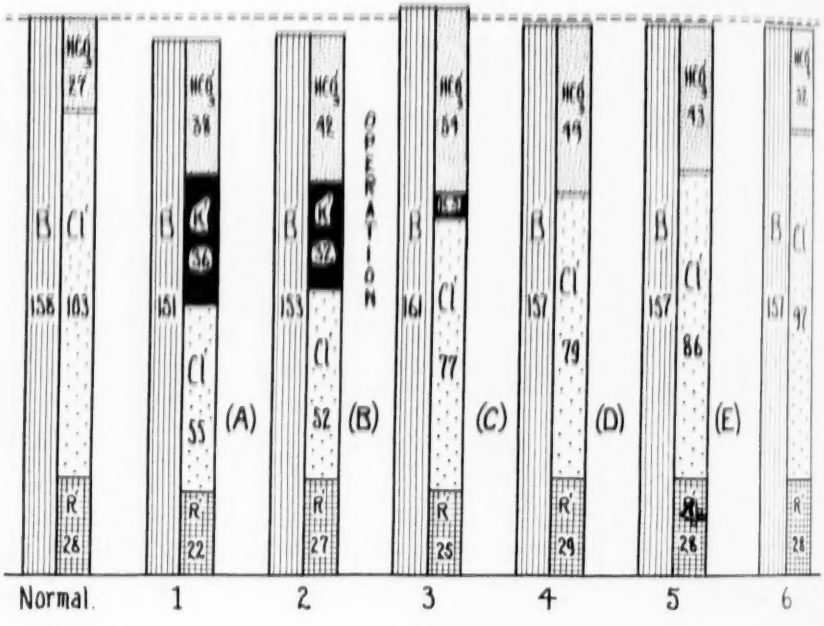


Chart 2.—Duodenal obstruction (case 1): The intervals between the sets of measurements and the therapeutic agents administered were as follows: (A) two days; 910 cc. of a 10 per cent solution of dextrose given intravenously, and 700 cc. of physiologic solution of sodium chloride given subcutaneously; (B) three days; 1,345 cc. of a 5 per cent solution of dextrose given intravenously, 3,075 cc. of physiologic solution of sodium chloride given subcutaneously and 1,730 cc. of 5 per cent dextrose in physiologic solution of sodium chloride given orally; (C) one day; 3,750 cc. of 5 per cent dextrose in physiologic solution of sodium chloride given by mouth; (D) one day; soft diet; (E) five days; soft diet.

and a considerable reduction of fixed base (B^*). These changes may be readily explained in terms of the clinical circumstances. The large loss of chloride ion and the smaller loss of fixed base are the result of the continued vomiting of gastric secretions. The ketosis is presumably due to the starvation which upper intestinal obstruction incidentally produces. Since, in the plasma, the ketone acids cover fixed base that would otherwise form bicarbonate, the presence of these

acids usually causes reduction of HCO'_3 below its usual value. Indeed, ketosis is by far the most frequent cause of acidosis. Here, however, the loss of chloride ion is larger than the accumulation of ketone acids, with the result that the bicarbonate ion concentration necessarily extends. In other words, there is alkalosis in the presence of ketosis. The diagram readily explains this somewhat unusual observation and shows that the presence of ketone acids in the urine should not be taken as establishing a diagnosis of acidosis. Incidentally, it is interesting to note the extent to which the ketone acids have limited bicarbonate increase; in their absence the large chloride recession would have produced a bicarbonate concentration of nearly double the value actually found. A smaller factor limiting bicarbonate is the loss of fixed base from the plasma. It may be mentioned that the reduction in the concentration of chloride ion and of fixed base in the blood plasma, as shown in the diagrams, by no means indicates the amounts of these materials withdrawn from the body. By means of experiments with rabbits, Gamble and McIver[9] demonstrated that, during the survival period following pyloric obstruction, the quantities of water, of fixed base and of chloride ion entering the stomach are actually several times the initial plasma content. Rapid and extensive replacement of these losses from the plasma by water and materials taken from the interstitial fluids of the body is thus indicated. It should therefore be borne in mind that the diagrams, although they show the changes produced in plasma structure by the losses of fixed base and of chloride ion, do not define the extent of their deficits within the body.

From the point of view of therapy, the plasma changes shown in diagram 1 present an interesting problem. One is asked to demolish the abnormal acids (A') and at the same time to rebuild the chloride ion concentration. Obviously if A' is reduced more rapidly than Cl' is raised, HCO'_3 must extend; in other words, the existing alkalosis will be increased. On the other hand, replacement of Cl' without adequate removal of A' will cause reduction of HCO'_3, possibly to the point of acidosis. The condition of this patient, however, so urgently required energetic administration of repair fluids that these theoretical considerations could not be dealt with experimentally. And it may be mentioned that repair of dehydration and reestablishment of renal function are much more important therapeutic ends than correction of the plasma bicarbonate. The results actually attained in the treatment of this patient are shown in the remaining diagrams. During the two days preceding the measurements shown in diagram 2, the patient received parenterally 700 cc. of physiologic solution of sodium chloride and 910 cc. of 10 per cent dextrose solution. As may be seen in the diagram, a slight reduction of the ketone acid concentration was obtained, but the amount of chloride supplied was not sufficient to replace even the current loss into the stomach. Obviously, the measures used were quantitatively inadequate. Much larger amounts of the repair fluids were given during the two following days: 3,075 cc. of salt solution and 1,345 cc. of 5 per cent dextrose solution. Operation was then performed and a complete obstruction, found just above the pancreatic duct, was relieved. The patient withstood the operation excellently, and there was no further vomiting. During the following twenty-four hours, 1,730 cc. of 5 per cent dextrose in physiologic solution of sodium chloride was given by mouth and was retained. The effects on plasma structure at the end of this three day period are shown in diagram 3. A considerable gain in chloride was obtained, and ketone acids were in large part removed. There was, however, further increase in bicarbonate, caused chiefly by a considerable rise in

9. Gamble, J. L., and McIver, M. A.: J. Clin. Investigation **1**:531, 1925.

fixed base. The patient at this point exhibited the slow shallow breathing characteristic of alkalosis; evidently, since no signs of tetany developed, this adjustment of respiration compensated to a considerable extent for the huge amount of plasma bicarbonate. During the next twenty-four hours 2,750 cc. of the 5 per cent dextrose in physiologic solution of sodium chloride was given by mouth, whereupon, as may be seen in diagram 4, the ketone acids entirely disappeared, there was further slight gain in chloride, the overreplacement of fixed base was corrected and the bicarbonate concentration was considerably reduced. At this point the general condition of the patient was excellent, renal function was active

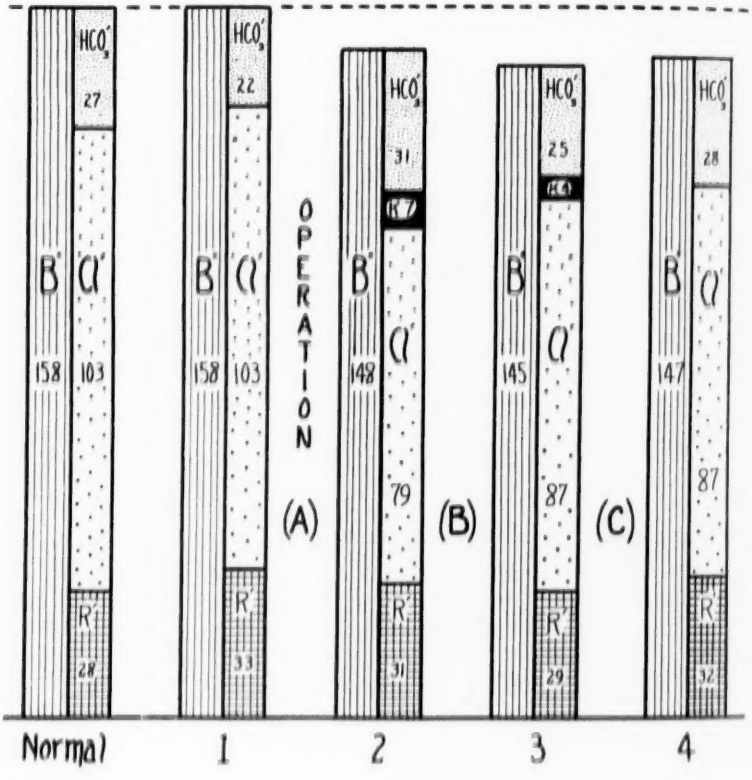


Chart 3.—Acute jejunal obstruction; volvulus (case 2): Intervals and therapeutic solutions given were as follows: (A) two days; 415 cc. of a 5 per cent solution of dextrose given intravenously; (B) one day; 700 cc. of physiologic solution of sodium chloride given subcutaneously; (C) one day; 1,050 cc. of physiologic solution of sodium chloride given subcutaneously; also, during (B) and (C), frequent small amounts of a mixture of orange juice, 5 per cent dextrose solution and physiologic solution of sodium chloride were given by mouth. The greater part was not retained.

and the gross evidences of dehydration had disappeared. Administration of salt solution was here discontinued and a suitable diet provided. Body fluid volume was undoubtedly completely reestablished although the chloride ion concentration

are still far below the mark. The loss of body water parallels the withdrawal of fixed base, chiefly sodium, from the body and is regained when the sodium deficit is repaired. Since this loss of sodium is much smaller than the accompanying loss of chloride ion, it will be replaced, when salt solution is given, long before that of chloride ion. We may therefore expect the restoration of body fluid volume to precede considerably the return of chloride ion concentration in the plasma to its usual level. By way of evidence on this point, it may be noted that the twenty-four hour specimen of urine, collected on the day corresponding to the plasma measurements given in diagram 6, was almost free from chlorides and was, moreover, alkaline (p_H 7.2), indicating the removal of surplus sodium as bicarbonate in order to permit retention of chloride ion.[8] The series of dia-

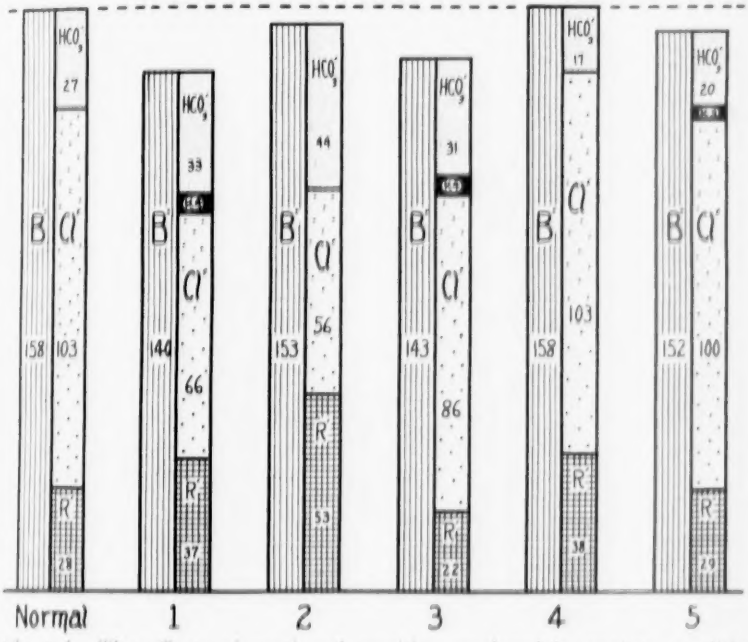


Chart 4.—The effects of continued vomiting produced by various conditions: column 1, pyloric stenosis; column 2, duodenal stenosis; column 3, neurotic vomiting; columns 4 and 5, intussusception.

grams excellently illustrates the size of the chloride ion deficit which may be produced by continued loss of gastric secretions. Even after the operation that put an end to the vomiting, the administration of nearly 5.5 liters of salt solution did not bring Cl' to its normal value, and at the end of a week on a diet containing a usual amount of chloride this mark was still not quite reached. Following the restoration of body fluid volume, repair of the chloride ion deficit could doubtless have been hastened by ingestion of hypertonic salt solution or by placing sodium chloride liberally in the diet.

Case 2.—*Volvulus of the Jejunum.*—In a boy, aged 6, acute obstruction of the lower jejunum developed following the operative removal of a portion of the bowel at the site of a lateral anastomosis which had been performed one year previously. The operation was undertaken for relief from symptoms of partial

obstruction. Vomiting began almost immediately afterward and, with occasional intermissions, continued until the death of the patient four days later. Volvulus was found at autopsy.

The measurements given in diagram 1 of chart 3 were obtained before operation and indicate that the condition of chronic partial obstruction which the patient presented at entrance, although it had caused occasional attacks of vomiting, had not established distortions of plasma structure. Diagram 2 shows the changes that developed during the two days following the operation, which consist, as may be seen, in an extensive fall of chloride ion and a considerable reduction of fixed base. No salt solution had been given during this interval. The only fluid supplied was an intravenous injection of 415 cc. of a 5 per cent solution of dextrose. This was not sufficient to prevent an accumulation of ketone acids. Owing to the very large loss of chloride ion, the bicarbonate was greatly extended, so that as in case 1, there was alkalosis in the presence of ketosis. The next day and the day following, 700 cc. and 1,050 cc., respectively, of physiologic solution of sodium chloride were given subcutaneously and produced slight gains of plasma chloride (diagrams 3 and 4). Small amounts of orange juice and of 5 per cent dextrose in salt solution were given frequently by mouth, and evidently, in spite of the vomiting, enough dextrose was absorbed to remove the ketone acids. The amounts of salt solution given were apparently sufficient to cover the rate of loss of fixed base and of chloride ion in vomited secretions but did not provide replacement of the amounts lost during the two days directly following the operation. These data may, therefore, serve to illustrate the importance of early and energetic administration of salt solution in the presence of circumstances producing continuous vomiting.

Case 3.—*Hypertrophic Stenosis of the Pylorus.*—The measurements recorded in diagram 1 of chart 4 are from the blood plasma of an infant that had vomited after feedings over a period of one month. They demonstrate excellently that hypertrophic stenosis of the pylorus may gradually produce the same changes of plasma structure, and to the same extent, as result rapidly in the presence of acute upper intestinal obstruction.

Case 4.—*Congenital Stricture of the Duodenum.*—The patient who provided the measurements given in diagram 2 of chart 4 was an infant, aged 3 weeks. Since birth there had been vomiting after feedings. At operation a stricture was found in the third portion of the duodenum. Again, the characteristic effect of loss of gastric secretions, extensive loss of chloride ion producing bicarbonate increase, is strikingly apparent in the diagram. The large increase in R′ is a common event in dehydration and is composed of an increase in the concentration of plasma protein together with a retention of its other component factors resulting from impairment of renal function.

Case 5.—*Neurotic Vomiting.*—A girl, aged 8 years, vomited vehemently after ingesting food or fluid. No organic cause could be found. Six days of this condition produced the plasma changes shown in diagram 3 of chart 4, which, as may be seen, were those of loss of stomach secretions together with the ketosis of fasting.

Cases 6 and 7.—*Intussusception.*—The two last diagrams in chart 4 are constructed from measurements obtained from infants about twelve hours after the onset of the symptoms of intussusception. There was no vomiting in one instance (diagram 4) and not a great deal of vomiting in the other (diagram 5). The only definite change of plasma structure in both was a moderate reduction of bicarbonate. Diagram 5 shows that this

was evidently due to ketosis. The ketone acids were not measured in the plasma represented by diagram 4 and are therefore included, if present, in R'. That there probably was ketosis of considerable degree is suggested by extension of this value. The urine, unfortunately, was not examined.

Diagrams 4 and 5 are not particularly informative, except as showing how rapidly ketosis may develop in infants and thereby indicating the early use of dextrose in such situations.

THE ACIDOSIS OF ADVANCED RENAL DISEASE

The diagram given in chart 1 shows the ionic composition of normal blood plasma. By controlling their entrance into the urine, the kidney is chiefly responsible for maintenance of the concentrations of the individual ions at the relative values indicated in the diagram, except in the case of bicarbonate ion and plasma protein. Bicarbonate ion, as we have noted, is established on the spot by the difference between the sum of the concentrations of the other acid factors and the total fixed base concentration. Since the usual size of the bicarbonate concentration thus depends on the concentrations of the other plasma ions being sustained at normal values, the kidney is also indirectly responsible for the bicarbonate concentration, although bicarbonate does not under ordinary circumstances enter the urine in appreciable amounts. Disturbances of renal function which result in alterations of various factors of plasma structure will thus inevitably cause a change in bicarbonate. It is therefore not surprising that in the presence of renal disease abnormal values for plasma bicarbonate are frequently found. Peters and his co-workers [10] thoroughly studied the alterations in the ionic composition of the blood plasma found in the presence of nephritis. An outstanding feature of their data is the great variability of the structural defects. The net result of the random changes in other factors is almost always in the direction of reduction in bicarbonate. Fortunately, the acidosis of nephritis is rarely of a degree requiring treatment except in the nearly terminal stage of the disease. Then, however, extremely severe acidosis producing distressing hyperpnea and evidently endangering life not infrequently develops. This can be relieved only by the intravenous injection of a solution of sodium bicarbonate. By this measure the hyperpnea can usually be removed and immediate death from acidosis prevented with the result that the patient is permitted to die of the orthodox terminal event, uremia. The measurements given in chart 5 illustrate the gross distortions of plasma structure resulting from advanced impairment of renal control and also demonstrate the futility of reparative attempts.

CASE 8. *Pyonephrosis.*—A girl, aged 7 years, exhibited severe hyperpnea on entrance to the hospital. The urine was found loaded with pus, and the non-

10. Peters, J. P.; Wakeman, A. M.; Eisenman, A. J., and Lee, C.: J. Clin. Investigation **6**:517, 1929.

protein nitrogen of the blood plasma was 171 mg. per hundred cubic centimeters. The initial measurements of the acid-base factors are represented by diagram 1, in which it may be seen that reduction of fixed base together with increase of chloride ion and R' very nearly demolished the bicarbonate. The patient was given 450 cc. of a 4 per cent solution of sodium bicarbonate intravenously. The effect was dramatic. Within half an hour her breathing, which had been distressfully deep and fairly rapid, became slow and shallow. Measurements taken sixteen hours later (diagram 2) showed complete restoration of bicarbonate. The extensive reduction of the chloride ion concentration seen in the diagram is presumably chiefly a dilution effect. During the second day after the administration of bicarbonate her breathing gradually increased in depth and rate, and by early

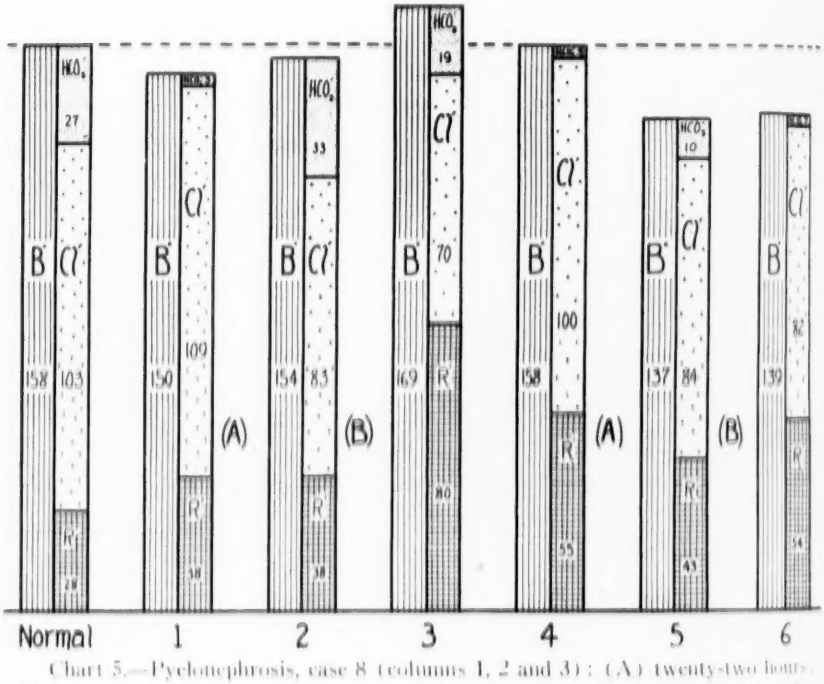


Chart 5.—Pyelonephrosis, case 8 (columns 1, 2 and 3): (A) twenty-two hours, 450 cc. of a 4 per cent solution of sodium bicarbonate given intravenously; (B) forty-eight hours; 400 cc. of a 4 per cent solution of sodium bicarbonate given intravenously. Chronic nephritis, case 9 (columns 4, 5 and 6): (A) eighteen hours; 1,300 cc. of a 5 per cent solution of dextrose given intravenously; 250 cc. of a 2 per cent solution of sodium bicarbonate given intravenously; (B) twenty-four hours; no solutions given.

morning of the third day she was as violently hyperpneic as on entrance to the hospital. Another injection of 4 per cent sodium bicarbonate solution (400 cc.) was then given, and four hours later, the measurements shown in diagram 3 were obtained. Fairly adequate replacement of bicarbonate is seen but at the expense of forcing the fixed base concentration above the correct value and of further reduction of chloride ion. During these two days there was rapid accumulation of the individually unmeasured acid factors producing an enormous extension of

R'. Six hours later, the convulsions of terminal uremia supervened. At autopsy both kidneys were found extensively destroyed by suppurative inflammation.

CASE 9.—*Chronic Nephritis.*—A girl, aged 13 years, on admission to the hospital had very great reduction of renal function as evidenced by the finding of 304 mg. of plasma nonprotein nitrogen per hundred cubic centimeters, and a phenolsulphonphthalein excretion of less than 1 per cent in two hours. There was extreme hyperpnea. As may be seen in diagram 4, normal values were found for the two chief factors of plasma structure, fixed base and chloride ion. The very small amount of bicarbonate is the result of a large extension of R' which is composed of the concentrations of the unmeasured acid factors. The plan of treatment used consisted in the intravenous administration of sodium bicarbonate and also in a large amount of additional fluid in the form of 5 per cent solution of dextrose, 800 cc. of dextrose solution being given first and followed, after an eight hour interval, by 250 cc. of a 2 per cent solution of sodium bicarbonate and 500 cc. more of the dextrose solution. Within one hour after injection of the bicarbonate solution the breathing was much reduced in rate and depth, and nine hours later the plasma bicarbonate was found to be considerably, though far from adequately, replaced (diagram 5). The large quantity of water given in the form of dextrose solution was apparently entirely ineffectual as a means of "flushing" the retained substances composing the increase of R' through the kidney. The large fall of the fixed base and chloride ion concentrations suggests that little of this fluid was excreted and that the decrease of R' is also a dilution effect. The extra fluid given thus produced only further great abnormality of plasma values. A third set of measurements given in diagram 6, obtained twenty-four hours later and about twelve hours before death, showed the blood plasma still diluted and further retention of the individually unmeasured acid factors almost obliterating bicarbonate.

SUMMARY

The data presented show the changes in the ionic composition of the blood plasma produced by continued vomiting and those found in the presence of advanced renal disease. The extent of repair obtained by the subcutaneous and intravenous injection of water and the substances indicated is also recorded by means of direct measurements of the chief factors of plasma structure.

EFFECTS OF INSULIN AND EPINEPHRINE ON THE BLOOD ACETONE IN FASTING CHILDREN *

LEIF SALOMONSEN, M.D.
OSLO, NORWAY

Clinical experience has fully established the antiketogenic effect of insulin in cases of diabetic ketosis, but the action of insulin in ketosis of nondiabetic origin is more uncertain. In adults living on a ketogenic diet, Herzberg [1] and Thannhauser and Mezger [2] found a decrease in ketosis after the administration of insulin. On the other hand, Burn and Ling [3] found an increase in ketonuria in fasting rats after the administration of insulin. In normal rabbits, Collip [4] has demonstrated that insulin can give rise to ketonuria, when the blood sugar falls as low as 0.065 and 0.045. Mainzer [5] has seen that insulin shock in diabetic patients may be accompanied by an increased excretion of ketone bodies. According to investigations made by Freise and his co-workers in children with alimentary and diabetic ketosis,[6] the antiketogenic action of the insulin arises only when the organism has a certain surplus of sugar at its disposal, whereas insulin increases or can produce ketosis in an organism that is poor in carbohydrates. On the basis of their experiments on rats, Burn and Ling arrived at conclusions that can be brought into harmony with this view, if, like Geelmuyden,[7] one regards the quantity of glycogen in the liver as being the antiketogenic factor. These authors conclude that insulin produces ketosis only when the quantity of glycogen in the liver is reduced.

An elucidation of the question is of both practical and theoretical importance, but great difficulties in obtaining this are encountered so long as in judging the individual results one has to deal with partly unknown, partly disputed processes of metabolism. It is not known what variations may exist with respect to these metabolic processes within the different species of animals and among animals in comparison with

* Submitted for publication, March 28, 1930.

* From the Municipal Hospital, Department VIII.

1. Herzberg, K.: Klin. Wchnschr. **3**:1816, 1924.

2. Thannhauser, S. J., and Mezger, H.: Klin. Wchnschr. **3**:1989, 1924.

3. Burn, J. H., and Ling, H. W.: J. Physiol. **65**:191, 1928.

4. Collip, J. B.: J. Biol. Chem. **55**:38, 1923.

5. Mainzer, F.: Klin. Wchnschr. **6**:107, 1927.

6. Freise, R., and Boeringer, H.: Monatschr. f. Kinderh. **32**:269, 1926. Freise, R., and Choremis, R.: Ibid. **31**:1, 1926.

7. Geelmuyden, H. C.: Acta med. Scandinav. **69**:381, 1929.

man and these variations may constitute one of the causes of the divergent results of experiments.

EXPERIMENTAL WORK

Experiments with Insulin.—In eight experiments on healthy fasting children, from 1 to 3 years old, the effect of small doses of insulin on blood sugar and blood acetone (acetone plus diacetic acid) has been investigated. The blood acetone was determined in 0.1 cc. of blood by the method of Widmark and the blood sugar by Hagedorn and Jensen's method.[8]

The experiments are arranged in order of succession according to the content of blood sugar at the beginning of the experiment. As is known, hunger itself brings about a rapid fall in blood sugar and considerable ketonemia in small children. The accompanying table shows

Blood Sugar and Blood Acetone Values

Duration of Fast, Hours	Blood Sugar, Gm. per 100 Cc.		Blood Acetone, Gm. per 100 Cc.	
	Mean Values	Minimum and Maximum Values	Mean Values	Minimum and Maximum Values
14	0.065	0.059 – 0.108	0.015	0 – 0.036
24	0.066	0.047 – 0.087	0.060	0.019 – 0.121
38	0.054	0.031 – 0.070	0.140	0.063 – 0.225
48	0.056	0.037 – 0.074	0.185	0.107 – 0.266
62	0.056	0.034 – 0.075	0.196	0.116 – 0.281

the mean and the extreme values for blood sugar and blood acetone during fasting periods of two days in fifteen children less than 3 years of age.

From these data it can be seen that insulin is administered when one knows by experience that the acetone curve is rising and the blood sugar curve is either falling or has reached its minimum value.

Although the valuation of the blood sugar curve is rendered difficult to some extent because it cannot be determined with certainty what part hunger plays in deciding the form of the curve, it undoubtedly appears from chart 1 that insulin produces a further fall in the already low blood sugar content, sometimes reducing it to extremely low values (0.019 Gm. per hundred cubic centimeters). At the same time, the rise of the blood acetone curve is unquestionably inhibited, which appears from a temporary, more or less great, decrease in the content of acetone in the blood. However, a distinct difference in degree is manifest—the lower the blood sugar content at the beginning of the experiment, the less marked is this effect; it appears later and is less pronounced. (In

8. Hagedorn, H. C., and Jensen, B. N.: Biochem. Ztschr. **135**:46, 1923.

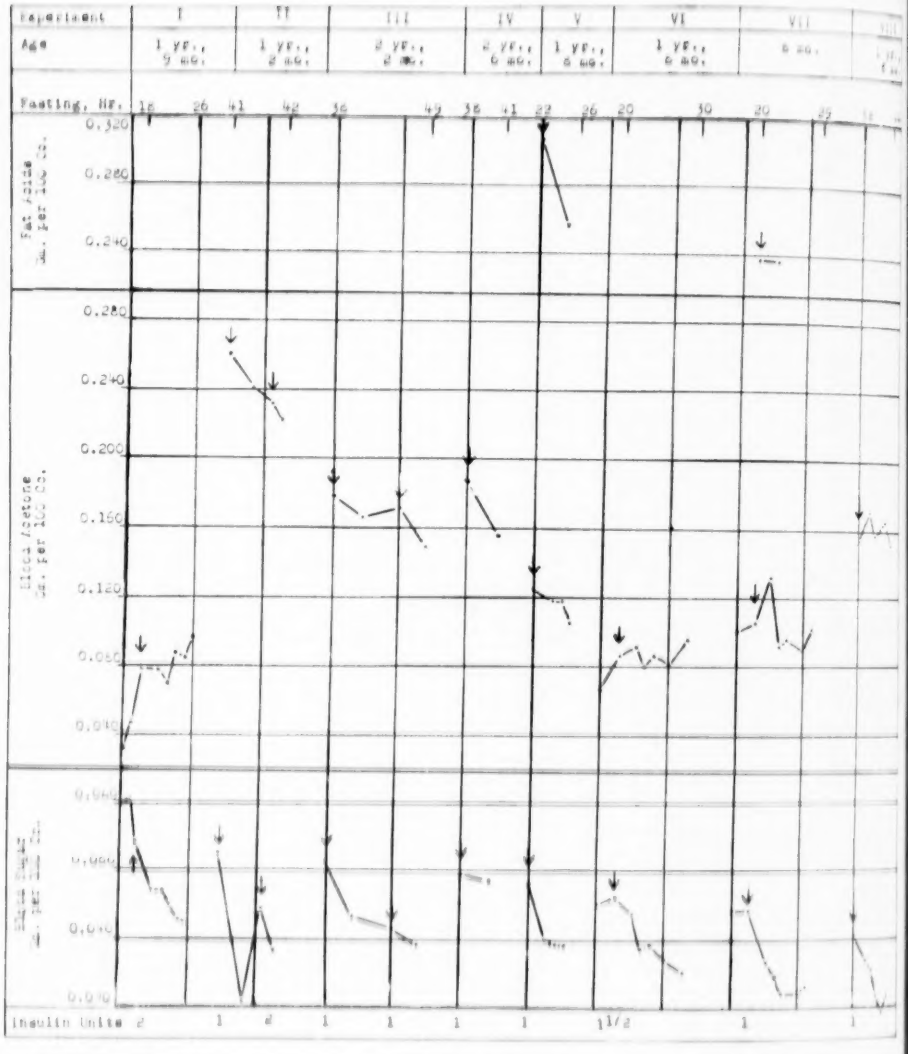


Chart 1.—Effect of injections of insulin on the blood sugar and acetone in children under 3 years of age.

experiment 1, the fact that the acetone curve is rising sharply at the time when the insulin is administered must be taken into account.)

In two experiments (5 and 7), the content of fatty acids in the blood plasma was determined before and after the administration of insulin.[9] In one of these experiments, a distinct decrease in lipemia occurred simultaneously with the fall in blood acetone. In the other experiments in which the acetone curve during the first two hours was continually rising, the quantity of fatty acids remained unaltered during these two hours.

Experiments with Epinephrine.—Epinephrine is known to be the pronounced antagonist of insulin in many respects. It would therefore be of interest to study the effect of epinephrine on the blood acetone under the same experimental conditions as in the experiments with insulin.

Hubbard and Wright [10] and Hirschhorn and Pollak [11] observed a rise in ketosis in nondiabetic persons after the administration of epinephrine. Anderson and Anderson [12] demonstrated that epinephrine in rats can increase an existing alimentary ketonuria. On the other hand, Burn and Ling [13] found that in the same species of animals epinephrine diminished the hunger ketonuria.

Seven experiments were performed on children less than 3 years of age. The epinephrine was injected subcutaneously in 0.1 per cent solution.

Like the experiments with insulin, those with epinephrine are arranged in order of succession according to the content of blood sugar at the commencement of the experiments.

9. Method: Fölling (Acta med. Scandinav., 1926, suppl. 651). By the same method there were found in six children of equal age the following values for the fatty acid content in blood plasma (grams per hundred cubic centimeters) during hunger:

Child	Duration of Fasting		
	14 hours	38 hours	62 hours
1	0.244	0.295	0.315
2	0.290	0.318	0.335
3	0.233	0.281	0.228
4	0.200	0.255	0.260
5	0.290	0.388	
6	0.269	0.299	

As seen, a constant and not inconsiderable rise in the quantity of fatty acids takes place in course of the first day of hunger.

10. Hubbard, R. S., and Wright, F. R.: J. Biol. Chem. **49**:385, 1921.
11. Hirschhorn, S., and Pollak, L.: Ztschr. klin. Med. **105**:371, 1927.
12. Anderson, A. B., and Anderson, M. D.: Biochem. J. **21**:1398, 1927.
13. Burn, J. H., and Ling, H. W.: J. Physiol. **64**:22, 1927.

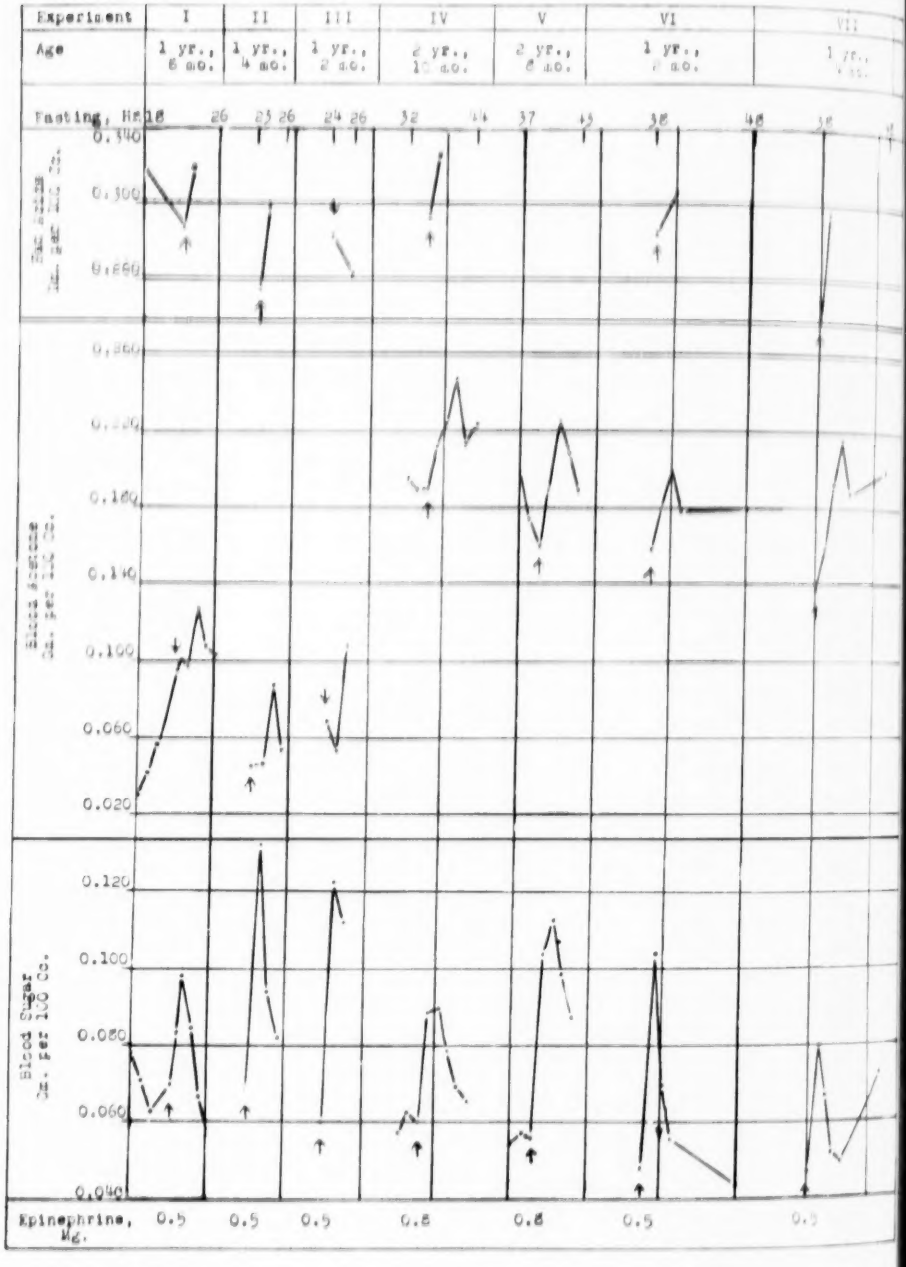


Chart 2.—Effect of injections of epinephrine on the blood sugar and acetone in children under 3 years of age.

In all the experiments the blood sugar showed an immediate rise, of considerable extent and of short duration, reaching the maximum one or two hours after the injection of epinephrine. In all cases there occurred a distinct, likewise temporary, rise in the acetonemia. The latter attains its maximum height, as a rule, one hour later than does the blood sugar. Just as in the experiments with insulin, there is also a difference in degree in the effect on the acetone curves: the lower the content of blood sugar, the greater and more rapid is the rise in acetonemia. In those cases in which epinephrine was given on the first day of fasting, at a time when the acetone curve, according to the results obtained in the pure hunger experiments, was rising most steeply, the epinephrine seems at first actually to inhibit this rise. This is in accordance with the fact that in the rats studied by Anderson and Anderson, the ketogenic action of the epinephrine was most distinctly evident in those animals in which the ketosis was high beforehand.

In five of six experiments a distinct rise in the quantity of fatty acids in the blood plasma occurs one hour (in experiment 6, two hours) after the injection of epinephrine.

These experiments show that the antagonism between insulin and epinephrine also manifests itself with regard to the hunger ketosis. So far, the two series of experiments may serve mutually to confirm each other.

COMMENT

The antiketogenic action of insulin is probably a purely secondary process, affectuated through the influence of insulin on sugar metabolism, possibly on fat and sugar metabolism. This is in harmony with the fact that the antiketogenic action in the experiments here reported manifests itself less distinctly the lower the content of blood sugar is, i. e., the less the amount of sugar that is actively at disposal for the metabolic processes. The presence of a certain quantity of sugar would therefore seem to be requisite in order that insulin may be able to reduce an existing ketosis.

To what phase of the sugar metabolism the insulin antiketogenesis is attached is, however, a question that is difficult to discuss, so long as one lacks a more intimate knowledge of the various influences of insulin on the metabolism of sugar. One is naturally led to think of an increased oxidation of dextrose. But it cannot be denied that the insulin antiketogenesis may be connected with another circumstance, namely, with an increased fixation of liver glycogen or with a restricted breakdown of fats. The considerable reduction in the content of fatty acids in the blood, which was observed in experiment 5, speaks—to some extent—in favor of a restriction in the transport of fat to the liver.

And the experiments with epinephrine may possibly point in the same direction, if one regards the epinephrine as being an antagonist of insulin. For even though the experiments with epinephrine afford no opportunity of drawing any certain conclusions, yet one has, as a working hypothesis, a reasonable explanation of the outcome of these experiments in the assumption that the epinephrine, directly or indirectly, occasions an increased transport of fat from the depots to the liver. The literature affords experimental data in support of such an assumption, for instance, in the experiments on dogs made by Junkersdorf and Török.[14] The rise in the content of fatty acids in the blood may find its explanation herein, likewise, the gradual increase in the ketogenic action, which occurs in proportion to the decrease in blood sugar: An increased transport of fat results in an increased production of ketone bodies, the normal further conversion of which is rendered difficult in proportion to the decrease of sugar in the organism.

SUMMARY

1. In fasting children less than 3 years of age an investigation was made on the effect of insulin and epinephrine on blood sugar, on blood acetone and on the content of fatty acids in the blood plasma during the hours immediately following the injections.

2. In eight experiments it was found that insulin reduces the blood acetone, but in decreasing degree according to the decrease of sugar in the organism. Epinephrine under the same conditions produces an increase in the blood acetone, the increase being greater in proportion as the organism is more poorly supplied with sugar.

3. In one experiment, insulin effected a distinct decrease in the content of fatty acids in the blood. In five of six experiments, injection of epinephrine was followed by a rise in the quantity of fatty acids.

14. Junkersdorf, P., and Török, P.: Arch. f. d. ges. Physiol. **211**:414, 1926.

THE PHYSIOLOGIC VARIATIONS IN THE INORGANIC BLOOD PHOSPHORUS CONTENT AT THE DIFFERENT AGE PERIODS

AN ATTEMPT TO EXPLAIN THESE IN THE GROWING CHILD*

J. K. BULLOCK, M.D.
NEW ORLEANS

Physiologic variation in the inorganic phosphorus content of the blood is a generally conceded fact. The blood of an infant is about twice as rich in phosphorus as adult blood; even at birth the blood phosphorus content has been found to be higher than that of the mother. But it is not definitely known what and where the phosphorus changes are, as the newly born infant passes through its infancy, childhood and adolescence to reach adult life with a blood phosphorus content of about one-half the original amount.

Of the inorganic constituents of the blood, calcium and phosphorus have proved to be the most important. The importance of these elements had been hinted by various authorities in the past, but their true relationship to each other and to certain bodily functions was not definitely established until comparatively recent times. The old authorities considered that rickets was a disease due to a deficiency in the calcium, but this idea has been gradually superseded by the fact that the inorganic phosphorus is most frequently at fault.

Most authorities have found that the inorganic phosphorus content of the blood ranges from 4 to 6 mg. per hundred cubic centimeters in normal children, and from 3 to 4 mg. in adults. The difference is thought to be due to the factor of growth. The ossification of the growth centers of the skeleton is thought to be completed at about the twentieth year. If the rate of growth depends on the rate of deposition of salt in the bones and this depends on the level of the inorganic phosphorus in the blood, one would expect to find the highest phosphorus levels at the three periods of maximum growth, viz., during the first six months, between 6 and 7 years, and at the age of puberty. Growth is more rapid in the first than in the second and third periods.

A tenable question would be: Does the content of inorganic phosphorus of the blood during the age periods of most active growth show an increase similar to the seasonal periods of most rapid growth? Also,

* Submitted for publication, April 16, 1930.

* From the Department of Pediatrics, Tulane University of Louisiana.

* Excerpt of a thesis offered to the Faculty of Graduate Studies, Tulane University, in partial fulfilment of the requirements for the degree of Master of Science, April 1, 1929.

does the relation between the content of inorganic phosphorus of the blood and the rate of growth remain the same during puberty and adolescence as in earlier childhood? And is there any difference in the variations in males and females?

With these wide variations in mind it occurred to me that it might be worth while to investigate more thoroughly the physiologic variations from birth to old age, and to try to ascertain to what extent these might be explained in the growing child.

REVIEW OF THE LITERATURE

Prior to 1920 the knowledge concerning the inorganic phosphorus of the blood was meager. Taylor and Miller,[1] Greenwald,[2] Marriott and Howland,[3] and Bloor[4] had published results of investigations on plasma in which several different methods were used. Denis and von Meysenbug[5] pointed out (1922) some possible errors in phosphorus determinations on plasma and suggested the use of serum whenever possible. In 1921, Howland, Kramer and Tisdall[6] made the statement that there is an increase in the inorganic phosphorus of the serum when allowed to stand in contact with the clot at room temperature. Later, Riesenfeld[7] concluded from his experiments that the differences in the inorganic phosphorus of the blood allowed to stand for one hour, and blood allowed to stand for twenty-four hours, in the refrigerator are insignificant, as they tend to balance each other. Maitland and Robinson[8] showed that the inorganic phosphorus in blood that had been laked with distilled water increased rapidly, as much as 10 per cent within five minutes and 50 per cent within two hours, when kept at room temperature.

The proportion of inorganic phosphorus is the same in serum and plasma. It contributes to the physiologic reaction and osmotic tension

1. Taylor, A. E., and Miller, C. W.: On the Estimation of Phosphorus in Biological Material, J. Biol. Chem. **28**:215, 1916-1917.

2. Greenwald, I.: Note on Determination of Inorganic Constituents of Blood and Other Physiological Material, J. Biol. Chem. **38**:439 (July) 1919.

3. Marriott, McK., and Howland, J.: Phosphate Retention, Arch. Int. Med. **18**:708 (Nov.) 1916.

4. Bloor, W. R.: Phosphates in Blood, J. Biol. Chem. **36**:49 (Oct.) 1918.

5. Denis, W., and von Meysenbug, L.: Note on a Possible Source of Error in the Bell-Doisy Method for the Determination of Phosphorus in the Blood Plasma, J. Biol. Chem. **52**: 1 (May) 1922.

6. Howland, J.; Kramer, B., and Tisdall, F. F.: The Clinical Significance of Calcium Concentration in the Serum of Children and Possible Errors in Its Determination, Am. J. Dis. Child. **22**:560 (Dec.) 1921.

7. Riesenfeld, E. A.; Handelman, L., and Rose, A. R.: Inorganic Phosphorus in the Blood of the Newly Born: Its Seasonal Variation and Relation to Rickets, Am. J. Dis. Child. **30**:646 (Nov.) 1925.

8. Maitland, Marjorie, and Robinson, Robert: Note on the Estimation of Phosphorus in Blood, Biochem. J. **18**:765, 1924.

of the serum. It is the chief factor in the metabolism of carbohydrates in the muscles, and physiologic experiments have shown that cerebral processes are very much under the influence of phosphorus acids.

While various authorities agree that the range of inorganic phosphorus in the serum of normal children is from 4 to 6 mg. per hundred cubic centimeters, McKellips, DeYoung and Bloor,[9] in 1921, obtained a range of from 1.2 to 4.6 mg. for infants from birth to 2 weeks of age. Wills,[10] in 1925, found an average of 4.8 mg. for five normal children between 5 and 10 years of age, with a range from 4.1 to 6.1 mg. In Tolstoi's[11] determination (1923) of the inorganic phosphorus of the serum of ninety-one adults, he obtained a range of from 2.5 to 3.3 mg. per hundred cubic centimeters. The age seemed to have no influence. Howland and Kramer,[6] in a series of normal infants and children between 3 months and 3 years of age, found (1921) an average of 6.1 mg. in the breast-fed infants and 5.1 mg. of those fed on cow's milk or a soft diet. The average for the entire group was 5.4 mg.

Williams,[12] working in New Orleans in 1928, found that the difference in age from 1 to 11 years made no difference in the amount of inorganic phosphorus in the blood. This work, however, was not limited to normal children. Von Meysenbug[13] reported (1922) an average of 5 mg. per hundred cubic centimeters in five nonrachitic infants from 1 to 19 months of age. In 1924, Anderson,[14] in a series of forty-nine children under 13 years of age, found an average of 4.7 mg. for those above 1 year and of 4.8 mg. for those under 1 year of age. There was no correlation between the age and the blood phosphorus content nor any diminution with advance in years. Buttinotti[15]

9. McKellips, G. M.; DeYoung, I. M., and Bloor, W. R.: The Distribution of Phosphoric Acid in the Blood of Normal Infants, J. Biol. Chem. **48**:53 (June) 1921.

10. Wills, L.: Blood Calcium and Inorganic Phosphorus in Children with Marked Lack of Muscle Tone, Brit. M. J. **1**:302 (Feb. 14) 1925.

11. Tolstoi, E.: The Inorganic Phosphorus of the Serum of Ninety-One Normal Adults as Determined by the Bell-Doisy Method, J. Biol. Chem. **55**:157 (Feb.) 1923.

12. Williams, C. T.: The Infrequency of Severe Rickets in New Orleans and Vicinity, with Attempt to Correlate Some of the Responsible Factors, Am. J. Dis. Child. **35**:590 (April) 1928.

13. Von Meysenbug, L.: The Inorganic Phosphorus Content of Breast Milk of Mothers with Normal and with Rachitic Children, Am. J. Dis. Child. **24**:200 (Sept.) 1922.

14. Anderson, G. H.: Phosphorus and Calcium in Normal and Rachitic Children, Brit. J. Child. Dis. **21**:33 (Jan.-March) 1924; 107 (April-June) 1924.

15. Carraban, J. P., and Buttinotti, S. I.: Phosphorus in the Blood, Semana méd. **34**:641 (March 17) 1927.

quoted Buckman as having shown that the inorganic phosphorus of the blood of the newly born is less than that of children over 1 year of age.

Howland and Kramer [16] found (1921) that all children with less than 3 mg. of phosphorus per hundred cubic centimeters of blood showed evidence of rickets. They contended that it is usually the low phosphorus content in rickets which prevents the normal deposition of calcium phosphate in the bones. Shipley, Park, McCollum and Simmonds,[17] in 1922, concluded that rickets may be due to either a diminution in the phosphorus or a diminution in the calcium. J. H. Hess and his co-workers [18] said that in moderate rickets the calcium or phosphorus or both may be lowered. In severe rickets the phosphorus is markedly reduced, while the calcium may or may not be reduced.

Hess and Lundagen [19] showed (1922) that there is a slight seasonal variation in the inorganic phosphorus of the blood of children which they considered a physiologic phenomenon. The highest level of the tide occurred in June and July and diminished steadily to reach the lowest in March.

Hess and Unger,[20] the year before, pointed out the marked similarity between the seasonal phosphorus curve and the curve of clinical rickets, and called attention to the fact that the peak of the rickets curve is coincident with the ebb of the phosphorus curve and vice versa. Park [21] said that the downward tendency in March may be simply an indication of the increased frequency, at this period of the year, of rachitic changes not sufficiently advanced to be demonstrated by ordinary clinical methods. Anderson [14] said that in no case did a low phosphorus content give an indication of rickets before other signs of the disease had been noted. Riesenfeld [7] (1925), in his work on new-born infants and their mothers, found that the phosphorus of the mother is more constant, there being no seasonal variation as is the case with the child. He stated that this may be a point in favor of the theory that seasonal variation is confined to rachitic or prerachitic cases, or occurs with seasonal variation in growth. Brunn [22] made monthly determinations (1928)

16. Howland, J., and Kramer, B.: Calcium and Phosphorus in the Serum in Relation to Rickets, Am. J. Dis. Child. **22**:105 (Aug.) 1921.

17. Shipley, P. G.; Park, E. A.; McCollum, E. V., and Simmonds, N.: Is There More Than One Kind of Rickets? Am. J. Dis. Child. **23**:91 (Feb.) 1922.

18. Hess, J. H.; Calvin, J. K.; Wang, Chi, and Fletcher, A.: Calcium and Phosphorus Determinations of the Blood in Rickets and Tetany, Am. J. Dis. Child. **26**:271 (Sept.) 1923.

19. Hess, A. F., and Lundagen, M. A.: Seasonal Tide of Blood Phosphate, J. A. M. A. **79**:2210 (Dec. 30) 1922.

20. Hess, A. F., and Unger, L. J.: Interpretation of the Seasonal Variation of Rickets, Am. J. Dis. Child. **22**:186 (Aug.) 1921.

21. Park, E. A.: Etiology of Rickets, Physiol. Rev. **3**:106 (Jan.) 1923.

22. Brunn, Karin: Seasonal Variations in the Phosphate Content of the Blood During the First Two Years of Life, Acta paediat. **7**:226 (April) 1928.

of the inorganic blood phosphorus in five infants throughout the year. There was no regular variation in the phosphate level, depending on the age of the subject; but in all the variations observed there occurred a pronounced sag in the curve during the first three or four months of the calendar year. These seasonal changes in Helsingsfors were more conspicuous than those reported by Hess in New York.

It has been conceded that cod liver oil and sunlight stimulate the concentration and retention of phosphorus in the blood, but it remained for Hess (1920) to systematize the use of heliotherapy in the treatment for rickets. Kramer, Casparis and Howland[23] found (1922) that rickets promptly heals when treated with the mercury vapor quartz lamp, with a gradual rise in the inorganic phosphorus of the blood. Koch and Caban[24] concluded from their experiments in 1927 that while cod liver oil raises the blood phosphorus to approximately normal limits, and while direct irradiation of the animal and the feeding of irradiated cholesterol have some influence in raising the phosphorus content of the blood, it is still possible to obtain a low phosphorus content and a low product of calcium and phosphorus in an animal which, so far as roentgenologic examinations can demonstrate, shows perfect calcification of the bones.

Bleyer[25] quoted the work of Malling and Hansen on the periodic variations in the growth of children. From their observations on the rate of growth they divided the year into three periods: a period of minimum growth, from mid-April to mid-July; a period of maximum growth, from mid-July to mid-December, and a period of mean growth, the so-called "rest period," from December to mid-April. The differences were found to be very great, growth in the maximum period being twice or even three times as great as that in the minimum period. Talbot[26] said that growth is most rapid at three different periods, viz., during the first six months, between 5 and 7 years, and at puberty. The rate is much more in the first than in the second and third cycles. The rate of growth varies in both weight and height. Growth in height is usually most rapid during the spring and the first half of summer. Growth in weight is most rapid during late summer and autumn. Female growth ceases and fat is deposited in certain parts of the body at 16 years. Male growth ceases at 21 or 22 years and deposits of fat are less pronounced.

23. Kramer, B.; Casparis, H., and Howland, J.: Ultra-Violet Irradiation in Rickets: Effects on the Calcium and Inorganic Phosphorus Concentration in the Serum, Am. J. Dis. Child. **24**:20 (July) 1922.

24. Koch, F. M., and Caban, M. H.: Inorganic Blood Phosphorus: Studies of Rats on Rachitic and Non-Rachitic Diets, Am. J. Dis. Child. **34**:187 (Aug.) 1927.

25. Bleyer, Adrian: Periodic Variation in the Growth of Infants, Arch. Pediat. **34**:366 (May) 1917.

26. Talbot, F. B.: Clinical Pediatrics, New York, D. Appleton & Company, 1920, ed. 8, p. 8.

In studying the literature on the ossification of bone, it can be said that ossification begins in utero in certain bones and is completed in the entire skeleton sometimes about the twentieth year. Cohn,[27] in numerous investigations on the subject, found that during the third year the head of the humerus increases rather rapidly in size, and that complete ossification within the coracoid is evident at the same time, while the tubercle of the tibia is not completely ossified and united to the shaft until the eighteenth year. From studying the work of Cohn,[27] Allen,[28] Engelbach[29] and others, one gathers that with the growth of the child the process of salt deposition shifts from one bone to the other, each age period being represented by a maximum deposit in some particular group of bones or epiphyses. With advance in age there is a decrease in the number of bones undergoing ossification, the last ones being completely ossified about the twentieth year. Some investigators give the age limit as high as 25 years. Allen[28] quoted Prior to the effect that bones of females ossify in advance of those of males.

Foote[30] stated that bones of infants in the first six months of life contain 60 per cent mineral matter, and that during the second year they contain 5 per cent more mineral matter than at birth. Adult bones contain 6 per cent more mineral matter than those of young infants.

In a study of the inorganic composition of bone in 1926, Howland, Marriott and Kramer[31] concluded that the calcium phosphate composition of all bones, rachitic and nonrachitic, is tricalcium phosphate. Different bones of the same person have the same composition. They pointed out that it has been shown that the ratio of calcium phosphate to calcium carbonate in rats is greater in the normal than in the rachitic animal, and that in certain of their analyses this may also obtain in rickets in human beings. The ratio of calcium phosphate to calcium carbonate, other things being the same, varies directly with the inorganic phosphorus content of the solution (experiments in vitro). The type of calcium phosphate compound is the same in the bones of rachitic and of nonrachitic children. It is also the same as that found in the bones of the newly born or in those of the adult.

27. Cohn, Isadore: Observations on the Normally Developing Shoulder, Am. J. Roentgenol. **8**:721 (Dec.) 1921; Observations on the Normally Developing Elbow, Arch. Surg. **2**:455 (May) 1921; Observations on the Normally Developing Knee, ibid. **5**:395 (Sept.) 1922.

28. Allen, Bundy: An X-Ray Study of the Development of the Ossification Centers of the Skeletal System, Radiology **7**:398 (Nov.) 1926.

29. Engelbach, W., and McMahan, A.: Osseous Development in Endocrine Disorders, Endocrinology **8**:1 (Jan.) 1924.

30. Foote, J. A.: Clinical Pediatrics, New York, D. Appleton & Company, 1927, vol. 7, p. 6.

31. Howland, J.; Marriott, McK., and Kramer, B.: Studies upon the Inorganic Composition of Bone, J. Biol. Chem. **65**:721 (June) 1926.

METHOD

Phosphorus determinations were made on persons from birth to old age. Children and adults were taken from the outpatient service and infants from the nursery for the newly born, Touro Infirmary, New Orleans. Persons with conditions that might have influenced the concentration of the inorganic phosphorus of the blood were eliminated from the series. All children aged 1 year or less were given cod liver oil and sunbaths as a routine procedure. Both breast-fed and bottle-fed babies were included. The bottle-fed babies were selected from those receiving well balanced formulas of either fresh cow's milk or dried milk. The older children had been following the routine dietary instructions of the clinic. In selecting the adults discrimination was made against those not receiving a fair amount of green vegetables.

In examination for rickets, the clincal points sought were: mild deformites of the bones, such as, eversion of the ribs at the infracostal margins, beading at the costochondral junctions, epiphysial enlargements at the wrists, flattening of the walls of the chest and first degree bowing of the legs, along with delayed dentiton and muscular weakness. Any one of the foregoing signs to a marked degree or any two to a mild degree were sufficient evidence to eliminate the subject from the series.

Persons of different ages were taken each month, in order that the general average would not be influenced by a possible seasonal variation. Determinations were made between May 1 and Nov. 1, 1928.

Blood was collected with a dry syringe by puncture of the longitudinal sinus or by venipuncture, and the inorganic phosphorus of the serum was determined within two and one-half hours. The blood was kept on ice until determinations were made.

The method employed was that of Fiske[32] for determination of inorganic phosphorus of the serum. Samples of blood were taken at about the same hour in each case: in the middle of the day before the noon meal, while the subject was at rest. In the case of the infants, it was impossible to collect the samples with any relation to nursing.

The inorganic phosphorus of the serum has been tabulated according to age and the average for the various ages represented graphically in the form of a curve.

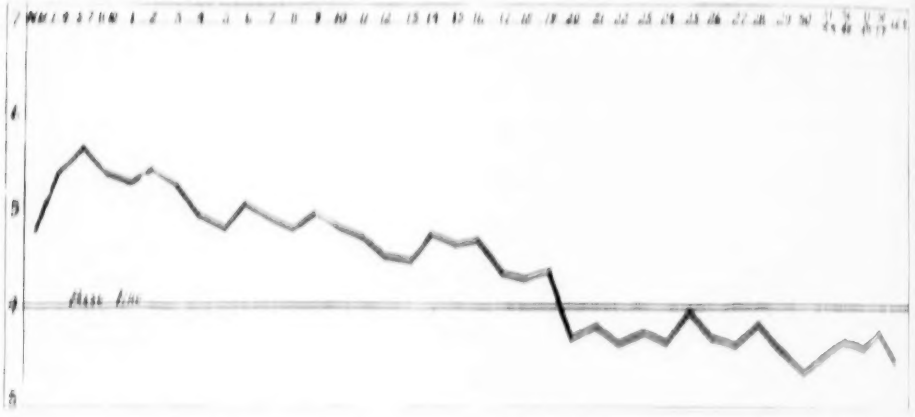
RESULTS

The inorganic phosphorus of the serum was determined in a total of 307 normal subjects, 139 of whom were males and 178 females; 170 were white and 137 were Negro subjects. The inorganic phosphorus range in the whole series was found to be from 6.81 to 2.50 mg.

32. Fiske, C. H., and Subbarow, Y.: Colorimetric Determination of Phosphorus, J. Biol. Chem. **66**:375 (Dec.) 1925.

per hundred cubic centimeters of serum. Fifty infants, ranging in age from 1 day to 10 months, gave an average of 5.33 mg., with a range of 6.81 to 3.81 mg. per hundred cubic centimeters. The average for the newly born infants was less than for any time under 5 years of age. The average for 121 subjects between 1 and 19 years of age was 4.77 mg., with a range of 5.92 to 3.57 mg. per hundred cubic centimeters. The total of 136 adults between 20 and 73 years of age averaged 3.65 mg., with a range of 4.85 to 2.5 per hundred cubic centimeters of serum.

It will be noticed from the curve that the averages are rather high for all ages. The table indicates that each age group shows a wide variation in figures, and that several of the figures for adults are higher than a few of the lowest for infants.



Curve of the inorganic phosphorus in the blood from birth to old age. The ordinates indicate milligrams of phosphorus per hundred cubic centimeters of serum, and the abscissae the age in months up to 10 and the age in years up to 60.

There occurs a rather rapid increase in the inorganic phosphorus from 4.82 mg. at birth to 5.06 mg. at the seventh month, which is the high peak in the curve. From this point there is a tendency for the phosphorus to decrease gradually with advance in age. While the fall is gradual up to the age of 19 years, at this point there is a more sudden drop. There are certain up and down fluctuations in the curve that are not definitely explainable.

The inorganic phosphorus of the serum of 136 adults ranged from 4.85 to 2.5 mg., which is a wider variation than that reported by Tolstoi.[1] His range for 91 adults was from 3.3 to 2.5 mg. per hundred cubic centimeters. However, in this series the figures above 4 mg. and below 3 mg. are extremely rare. None of the age groups above 20

Determinations of the Inorganic Phosphorus in the Blood from Birth to old Age

Case	Age	Mg. of Phosphorus per 100 Cc. of Serum	Sex	Race	Month, 1928
1	3 days	3.81	M	W	November
2	5 days	4.92	M	W	November
3	6 days	5.33	M	W	June
4	9 days	4.57	F	W	October
5	8 days	4.85	M	W	July
6	3 days	5.93	F	W	July
7	2 days	5.00	F	W	August
8	1 day	5.71	F	W	September
9	8 days	4.80	M	W	September
10	2 days	5.85	F	W	October
11	3 days	5.19	F	W	May
12	4 days	5.24	M	W	June
13	0 days	4.62	M	W	October
New born, average		4.82			
14	1 month	4.80	F	C	May
15	1 month	4.77	M	C	May
16	1 month	5.53	F	C	August
17	1 month	5.71	F	C	June
18	2 months	5.33	M	W	October
19	2 months	5.52	M	W	June
20	2 months	6.15	M	C	May
21	2 months	4.50	F	W	September
22	3 months	6.66	F	W	August
23	3 months	5.33	M	W	May
24	3 months	5.71	F	C	July
25	3 months	5.71	M	C	July
26	4 months	6.15	F	W	May
27	4 months	5.00	M	W	May
28	4 months	5.52	M	W	August
29	4 months	5.93	F	W	September
1 to 4 months, average		5.47			
30	5 months	5.93	M	W	October
31	5 months	5.71	M	C	August
32	5 months	6.08	M	W	May
33	6 months	6.42	F	W	June
34	6 months	4.00	M	W	June
35	6 months	4.83	F	C	July
36	6 months	6.09	M	W	June
37	6 months	5.55	M	W	August
38	6 months	5.33	F	W	October
39	7 months	5.71	M	C	September
40	7 months	6.66	F	C	May
41	7 months	5.93	F	C	September
5 to 7 months, average		5.66			
42	8 months	6.15	F	W	July
43	8 months	5.16	F	C	May
44	8 months	5.33	M	W	May
45	9 months	6.26	M	W	May
46	9 months	5.33	M	W	October
47	10 months	5.26	M	C	July
48	10 months	5.00	F	W	September
49	10 months	4.57	M	C	September
50	10 months	5.26	F	C	June
8 to 10 months, average		5.41			
51	1 year	5.71	M	C	May
52	1 year	5.00	M	W	June
53	1 year	5.26	F	W	October
1 year, average		5.33			
54	2 years	4.70	M	C	September
55	2 years	5.82	F	C	May
56	2 years	6.71	F	C	June
57	2 years	5.63	F	C	September
2 years, average		5.46			

Determinations of the Inorganic Phosphorus in the Blood from Birth to Old Age—Continued

Case	Age	Mg. of Phosphorus per 100 Cc. of Serum	Sex	Race	Month, 1925
58	3 years	5.33	M	C	May
59	3 years	5.33	F	W	June
60	3 years	4.44	F	C	September
61	3 years	5.00	M	W	October
62	3 years	5.71	F	C	May
63	3 years	5.92	F	W	May
3 years, average		5.29			
64	4 years	4.57	F	C	May
65	4 years	5.00	F	C	May
66	4 years	5.61	M	C	June
67	4 years	4.57	M	W	June
68	4 years	4.44	F	C	June
69	4 years	5.71	F	C	June
70	4 years	5.52	F	W	June
71	4 years	4.21	M	W	July
72	4 years	4.57	M	W	July
73	4 years	5.71	M	C	October
4 years, average		4.98			
74	5 years	5.16	M	W	May
75	5 years	4.85	M	W	May
76	5 years	4.70	F	W	July
77	5 years	4.10	F	W	September
78	5 years	4.44	F	W	October
79	5 years	4.70	M	C	October
80	5 years	5.71	F	W	September
5 years, average		4.81			
81	6 years	5.08	M	C	May
82	6 years	5.00	F	W	June
83	6 years	4.85	M	W	August
84	6 years	4.70	F	C	June
85	6 years	5.33	F	W	October
86	6 years	5.52	F	W	October
6 years, average		5.08			
87	7 years	5.00	F	W	May
88	7 years	4.44	F	W	May
89	7 years	4.77	M	C	June
90	7 years	5.33	M	W	July
91	7 years	5.33	F	C	October
92	7 years	4.70	F	W	October
7 years, average		4.93			
93	8 years	5.00	M	W	May
94	8 years	5.33	F	C	May
95	8 years	4.10	F	C	May
96	8 years	5.00	M	W	June
97	8 years	4.92	F	W	June
98	8 years	5.71	F	W	July
99	8 years	5.33	F	W	August
100	8 years	4.21	M	W	August
101	8 years	5.33	M	W	August
102	8 years	3.62	F	C	September
103	8 years	4.70	F	W	October
104	8 years	4.92	F	W	May
8 years, average		4.83			
105	9 years	5.33	F	W	May
106	9 years	4.70	F	W	May
107	9 years	6.00	F	W	May
108	9 years	4.44	F	W	June
109	9 years	6.00	M	W	July
110	9 years	4.07	F	W	August
111	9 years	6.74	M	W	August
112	9 years	4.07	F	W	September
113	9 years	6.33	M	W	October
9 years, average		5.00			

Determinations of the Inorganic Phosphorus in the Blood from Birth to Old Age—Continued

Case	Age	Mg. of Phosphorus per 100 Cc. of Serum	Sex	Race	Month, 1928
114	10 years	5.00	M	W	June
115	10 years	5.33	F	W	July
117	10 years	4.21	F	W	October
118	10 years	4.85	M	W	October
10 years, average		4.85			
119	11 years	4.26	M	C	May
120	11 years	5.08	M	W	May
121	11 years	5.16	F	W	May
122	11 years	4.70	M	W	August
123	11 years	5.33	M	W	August
124	11 years	5.00	M	W	August
125	11 years	4.21	M	C	September
126	11 years	3.62	F	C	September
127	11 years	5.00	F	C	September
11 years, average		4.71			
128	12 years	4.21	M	W	May
129	12 years	3.95	F	W	June
130	12 years	4.00	F	W	June
131	12 years	5.16	F	C	July
132	12 years	5.33	M	W	August
133	12 years	4.44	F	C	September
12 years, average		4.51			
134	13 years	4.10	F	C	May
135	13 years	5.00	F	W	June
136	13 years	4.44	M	W	October
137	13 years	4.32	F	W	September
13 years, average		4.46			
138	14 years	4.77	M	W	May
139	14 years	4.00	F	W	June
140	14 years	4.70	M	W	July
141	14 years	5.00	F	W	October
142	14 years	5.33	M	W	October
14 years, average		4.76			
143	15 years	4.00	M	C	May
144	15 years	4.50	M	W	June
145	15 years	5.16	F	C	August
146	15 years	5.00	M	W	September
147	15 years	4.70	F	W	September
15 years, average		4.67			
148	16 years	4.70	M	C	August
149	16 years	5.00	F	C	May
150	16 years	4.44	F	W	June
151	16 years	4.57	M	C	September
16 years, average		4.68			
152	17 years	3.57	F	C	May
153	17 years	4.85	M	W	June
154	17 years	4.44	F	C	August
155	17 years	4.21	F	C	October
156	17 years	4.70	M	W	October
17 years, average		4.35			
157	18 years	4.85	M	C	May
158	18 years	4.00	M	W	May
159	18 years	3.81	F	W	June
160	18 years	4.21	F	C	August
161	18 years	4.44	M	W	August
162	18 years	4.08	F	C	September
163	18 years	4.09	F	C	September
164	18 years	4.44	M	C	September
18 years, average		4.31			

Determinations of the Inorganic Phosphorus in the Blood from Birth to Old Age—Continued

Case	Age	Mg. of Phosphorus per 100 Cc. of Serum	Sex	Race	Month, 1908
165	19 years	4.44	F	C	June
166	19 years	4.21	F	C	August
167	19 years	4.00	F	W	August
168	19 years	4.00	M	W	August
169	19 years	4.85	M	C	September
170	19 years	4.00	F	W	October
171	19 years	4.85	M	C	October
19 years, average		4.37			
172	20 years	4.00	M	C	July
173	20 years	3.20	F	W	July
174	20 years	3.33	F	C	September
175	20 years	3.62	F	C	June
176	20 years	4.21	M	W	September
20 years, average		3.67			
177	21 years	2.90	M	W	May
178	21 years	3.72	M	C	July
179	21 years	4.10	M	C	July
180	21 years	3.50	F	C	July
181	21 years	3.50	F	W	July
182	21 years	2.80	M	W	August
183	21 years	4.70	F	C	August
184	21 years	4.80	M	W	September
185	21 years	4.00	F	C	September
186	21 years	3.72	F	C	September
21 years, average		3.80			
187	22 years	3.72	M	W	May
188	22 years	3.48	M	C	May
189	22 years	3.07	F	W	June
190	22 years	4.44	F	W	August
191	22 years	3.48	M	W	October
22 years, average		3.64			
192	23 years	3.55	F	C	May
193	23 years	4.21	F	C	June
194	23 years	3.48	M	W	July
195	23 years	2.86	M	W	July
196	23 years	2.96	M	W	August
197	23 years	3.81	F	W	August
198	23 years	4.44	F	C	September
199	23 years	4.32	M	C	September
200	23 years	3.51	F	C	September
201	23 years	4.21	M	C	September
23 years, average		3.73			
202	24 years	4.32	M	W	May
203	24 years	2.66	F	W	June
204	24 years	3.90	F	C	June
205	24 years	4.32	F	C	July
206	24 years	3.81	F	C	July
207	24 years	3.62	F	W	August
208	24 years	3.48	M	W	September
209	24 years	2.50	M	W	August
210	24 years	4.00	F	W	September
211	24 years	3.36	F	W	September
212	24 years	3.90	M	C	September
24 years, average		3.62			
213	25 years	4.26	F	C	May
214	25 years	3.07	F	W	June
215	25 years	4.70	F	C	June
216	25 years	3.62	F	W	July
217	25 years	4.57	F	C	September
218	25 years	3.03	F	C	September
25 years, average		3.96			

Determinations of the Inorganic Phosphorus in the Blood from Birth to Old Age—Continued

Case	Age	Mg. of Phosphorus per 100 C.c. of Serum	Sex	Race	Month, 1938
[illegible]	26 years	3.67	M	W	May
[illegible]	26 years	4.05	F	C	May
[illegible]	26 years	4.00	F	C	June
[illegible]	26 years	3.13	F	C	August
[illegible]	26 years	3.48	F	W	August
[illegible]	26 years	3.51	M	C	August
[illegible]	26 years	3.62	M	C	September
[illegible]	26 years	4.00	M	W	September
26 years, average		3.68			
[illegible]	27 years	3.36	M	C	May
[illegible]	27 years	3.74	F	W	May
[illegible]	27 years	3.07	F	C	May
[illegible]	27 years	3.85	M	C	June
[illegible]	27 years	4.21	F	W	June
[illegible]	27 years	3.03	F	W	June
[illegible]	27 years	3.90	M	W	July
[illegible]	27 years	3.62	M	C	September
[illegible]	27 years	4.21	F	C	September
[illegible]	27 years	3.33	M	C	September
27 years, average		3.81			
[illegible]	28 years	3.51	M	W	June
[illegible]	28 years	4.44	M	C	June
[illegible]	28 years	3.70	M	C	June
[illegible]	28 years	3.81	F	W	July
[illegible]	28 years	3.81	F	W	September
[illegible]	28 years	3.48	F	W	September
[illegible]	28 years	4.00	M	C	September
[illegible]	28 years	3.43	F	W	September
[illegible]	28 years	4.21	F	C	October
[illegible]	28 years	3.33	F	C	October
28 years, average		3.79			
[illegible]	30 years	3.07	M	W	June
[illegible]	30 years	3.81	M	C	July
[illegible]	30 years	3.43	M	C	September
[illegible]	30 years	4.10	M	W	September
30 years, average		3.60			
[illegible]	30 years	3.29	F	W	July
[illegible]	30 years	3.07	F	W	July
[illegible]	30 years	3.58	M	W	September
[illegible]	30 years	4.32	M	C	September
30 years, average		3.31			
[illegible]	31 years	3.62	M	W	June
[illegible]	32 years	3.33	M	C	September
[illegible]	32 years	3.16	M	C	September
[illegible]	32 years	3.81	M	W	September
[illegible]	33 years	3.85	F	C	June
[illegible]	33 years	3.33	F	W	October
[illegible]	34 years	3.62	F	C	September
[illegible]	34 years	3.20	F	W	May
[illegible]	35 years	3.57	M	C	May
[illegible]	35 years	3.48	F	C	September
31 to 35 years, average		3.49			
[illegible]	36 years	4.70	F	W	August
[illegible]	36 years	3.62	F	W	August
[illegible]	36 years	3.02	M	W	May
[illegible]	37 years	4.21	M	C	June
[illegible]	37 years	3.26	F	C	June
[illegible]	37 years	3.81	M	W	May
[illegible]	39 years	4.00	F	W	August
[illegible]	39 years	3.20	F	C	June
[illegible]	40 years	3.62	M	C	August
[illegible]	40 years	3.02	F	C	August
[illegible]	40 years	3.13	F	W	June
[illegible]	40 years	4.44	M	C	May
[illegible]	40 years	3.90	M	C	May
[illegible]	40 years	3.48	F	W	July
36 to 40 years, average		3.63			

Determinations of the Inorganic Phosphorus in the Blood from Birth to Old Age—Continued

Case	Age	Mg. of Phosphorus per 100 Cc. of Serum	Sex	Race	Month, 1928
278	41 years	3.81	F	C	July
279	41 years	3.72	F	C	July
280	41 years	3.48	M	W	August
281	43 years	3.55	F	W	June
282	43 years	3.02	F	C	September
283	44 years	3.33	M	C	June
284	44 years	3.40	F	W	September
285	44 years	3.48	F	C	September
286	48 years	4.00	M	W	May
287	48 years	3.90	M	C	June
288	48 years	2.58	F	C	July
289	49 years	3.85	M	W	June
290	49 years	4.26	F	C	August
291	49 years	3.33	F	C	August
41 to 49 years, average		3.55			
292	50 years	3.33	M	C	July
293	51 years	3.23	M	W	May
294	51 years	3.90	F	C	June
295	51 years	2.96	M	W	July
296	51 years	4.10	M	W	September
297	52 years	3.72	F	W	June
297	52 years	4.21	M	C	September
299	54 years	3.95	M	C	May
300	56 years	3.72	M	W	May
301	56 years	3.62	F	C	August
302	57 years	4.15	F	C	September
50 to 57 years, average		3.72			
303	62 years	2.26	F	W	June
304	67 years	3.51	M	W	May
305	67 years	3.40	F	C	July
306	69 years	3.93	M	C	June
307	73 years	3.07	M	C	June
60 + years, average		3.40			

years averaged as much as 4 mg., which represents the base line for the curve. There were quite a few persons with values above 4 mg., even some in the old age groups.

In averaging separately the results for the males and females, it was found that some ages were not represented, or that there were not enough cases to justify a conclusion. According to the figures present, however, there is a tendency for the figures for female subjects from about 10 or 11 to 13 years to run a little lower than those for male subjects, indicating that the earlier termination of female growth at about 16 years may bear some relation to the phosphorus content of the blood.

COMMENT

From the results of this investigation, the conclusion is drawn that the inorganic phosphorus content of the serum increases rather rapidly during the first half of the first year of life, reaching its highest peak at the sixth or seventh month. From this point the serum phosphorus decreases gradually, with various slight fluctuations, to reach a constant quantity at the time of termination of osseous growth, which is about the twentieth year. From this age the phosphorus content of the blood is more or less constant.

It will be noticed from the table, as stated before, that the average for each age group is rather high. Determinations were made during the high tide of seasonal variations, from May through September. This, no doubt, is a big factor in accounting for the generally high values for the entire series as compared with those found in other localities. This is in keeping with the results obtained by Williams [12] in 1928. He stated that the phosphorus level is higher at all times during the year in New Orleans than it is in New York. Williams found a variation of 1 mg. per hundred cubic centimeters between the summer and winter levels in New Orleans. Also, Bruun [22] found a much more conspicuous variation in Helsingsfors than that reported by Hess for New York, while Anderson [14] did not find a seasonal variation in Glasgow.

It has been stated by various authorities that the normal inorganic phosphorus content of the blood is about 5 mg. per hundred cubic centimeters of serum in the child, and about 3 mg. per hundred cubic centimeters of serum in the adult. This difference has been explained as follows: Up to the age of 20 years, the phosphorus content remains constant; after that it is reduced to a lower level, which remains unchanged during the rest of life. This abrupt change is supposed to mark the termination of osseous growth. The question here arises, as to the rapidity with which growth ceases. According to Talbot,[23] growth is most rapid at three different periods: during the first 6 months, between 5 and 7 years, and at puberty. The rate of growth, as stated by Howland,[33] depends on the rate of deposition of salts in the bones, and this depends on the level of the inorganic phosphorus in the blood. In this series the most striking increase in the blood phosphorus was found during the period of most rapid growth, viz., the first six months of life. The gradual decrease that occurred in the inorganic phosphorus of the blood from the first 6 months to the age of 19 years indicates that the rate of deposition of salts in the bones is not constant, but decreases with advance in years. It has been shown that the amount of mineral matter increases 5 per cent during the first two years and only 3 per cent during the remainder of life, and that the type of calcium phosphate is the same in the bones of infants as in those of adults.

At 19 years of age the more rapid decrease in the content of inorganic phosphorus is, no doubt, related to the cessation of bony growth and is comparable to the rapid rise that occurs during the first half year of life which is the period of the beginning rapid growth. The second and third periods of most active growth are not represented by an

33. Howland, J.: The Etiology and Pathogenesis of Rickets, Harvey Lectures, Philadelphia, J. B. Lippincott Company, 1922-1923, vol. 18, p. 189.

appreciable varaition in the phosphorus curve; however, this does not mean that a slight increase is not present. The comparatively greater rate of growth in the first than in the second and third cycles would be expected to show a correspondingly greater increase in the inorganic phosphorus of the blood. Thus, it may be said that the increase in phosphorus is not as rapid and as marked for the age periods of most rapid growth as for the seasonal periods of most rapid growth.

From the figures available among the two sexes, it is suggested that females show a more rapid decrease in the blood phosphorus at about 16 and 17 years. This is in agreement with the idea that female growth is in advance of male growth and that it is probably completed two or three years sooner. However, some of the determinations on male and female subjects who were well advanced in years show values above 4 mg.

There are numerous up and down fluctuations in the curve that are not interpreted to be of any significance, but that are probably due to individual variatons combined with slight errors that occur in determinations. It is of impotance also that in this series the average does not represent the same number of subjects for the different ages.

SUMMARY

1. The variation in the content of inorganic phosphorus in the blood during the different age periods of life has been verified.

2. The phosphorus content of the blood of infants increases rather rapidly during the first half of the first year, reaching its peak at the sixth or seventh month, and then diminishing gradually until the time of termination of osseous growth, at about the nineteenth or twentieth year, after which it remains more or less constant.

3. The phosphorus content of the blood of newly born infants was found to be less than that for any age group under 5 years.

4. The phosphorus levels of the different age groups of this series are rather high as compared with the results of others in different localities. The season of the year at which these determinations were made probably influenced these higher levels to a certain extent.

5. The age periods of most rapid growth do not show as marked an increase in the inorganic phosphorus as do the seasonal periods of most rapid growth.

6. It is suggested that females show a more rapid decrease in the blood phosphorus at about 16 or 17 years than do males.

7. It would seem reasonably certain from the results herein reported that there is a significant relationship between the high phosphorus levels and the age periods of most active growth.

CEREBROSPINAL FLUID OF PREMATURE INFANTS

RESULTS OF A SERIES OF SPINAL PUNCTURES IN ONE HUNDRED AND SEVENTY CASES, WITH SPECIAL REFERENCE TO THE ORIGIN OF PHYSIOLOGIC XANTHOCHROMIA OF THE NEW-BORN INFANT *

JEROME GLASER, M.D.
ROCHESTER, N. Y.

Some time ago the results of a series of spinal punctures on 100 premature infants were published and discussed with particular reference to intracranial hemorrhage and pigmentation of the cerebrospinal fluid.[1] Since then the series has been increased to 170 infants. In general, though there have been but few changes in the conclusions advanced in the first paper, the conditions observed in the second series of 70 infants, together with a theory that has been developed in the course of the work to explain physiologic xanthochromia of the new-born infant, are sufficiently interesting to warrant publication. In the discussion to follow, the term "meningeal" hemorrhage will be used instead of "cerebral" or "intracranial," as the former term more accurately designates the pathologic condition under consideration.

TECHNIC

The technic previously described for lumbar puncture in premature infants has continued satisfactory. In brief, this consists in using a small hypodermic needle (no. 27) for performing the puncture and having the infant held in a sitting position so that the lumbar portion of the dural sac is distended by pressure from above of the column of fluid within it. This helps to avoid the most common cause of faulty lumbar punctures in premature infants, the detachment of the posterior wall of the spinal dura mater by the entering needle and the pushing forward of this posterior wall against the anterior wall, resulting in a dry tap, or a bloody tap if both dural walls are pierced and the posterior vertebral venous plexus is injured. This is doubtless responsible for many faulty taps for which no adequate explanation is found when necropsy is performed in the usual manner, as, for example, in the series of Waitz.[2]

* Submitted for publication, April 5, 1930.

* From the Leon Klein Fund, the Premature Infant Station of the Sarah Morris Hospital for Children and the Nelson Morris Institute for Medical Research of the Michael Reese Hospital, Chicago.

1. Glaser, J.: The Cerebrospinal Fluid of Premature Infants, with Special Reference to Intracranial Hemorrhage and Pigmentation, Am. J. Dis. Child. **36:** 195 (Aug.) 1928.

2. Waitz, R.: Le liquide céphalorachidien du nouveau-né, Rev. franç. de pédiat. **4:**1 (Feb.) 1928.

EXPERIMENTAL DATA

The material from which this study was made is briefly recapitulated in table 1. All infants in the series had a history of less than forty weeks' gestation and a birth weight of 2,500 Gm. or less. Neither age nor weight was considered a contraindication to lumbar puncture in cases of suspected meningeal hemorrhage.

Table 2 indicates that in this series of 94 necropsies gross meningeal hemorrhage or acute meningeal congestion was present in 35 instances, or 37 per cent. Of these 35 infants, the spinal fluid was grossly bloody or hazy in 28, or 80 per cent of cases. By way of definition, it may be

TABLE 1.—*Summary of Cases*

	First Series		Second Series		Total	
	No. of Cases	Per-centage	No. of Cases	Per-centage	No. of Cases	Per-centage
Premature infants	100	..	70	..	170	..
Deaths	81	81	29	41	110	65
Necropsies	70	86	24	82	94	85
Total lumbar punctures	129	..	77	..	206	..
Punctures on living infants	63	49	53	70	116	56

TABLE 2.—*Meningeal Hemorrhage or Acute Meningeal Congestion Present at Necropsy*

	First Series		Second Series		Total	
	No. of Cases	Per-centage	No. of Cases	Per-centage	No. of Cases	Per-centage
Spinal fluid grossly bloody or hazy	19	73	9	100	28	80
Spinal fluid clear	7	27	0	0	7	20

said that a hazy fluid is one which owes its appearance to the presence of red blood cells which are not present in sufficient number to cause a pink color but are present in sufficient number, at least 500 per cubic millimeter, to prevent the fluid from being classified as "water clear." The 7 instances in which gross meningeal hemorrhage was found at necropsy without bloody cerebrospinal fluid occurred in the first series of 100 infants. The fact that no clear fluids were found in meningeal hemorrhage in the second series is possibly due to the paucity of cases but may perhaps be attributed to the fact that while this series was being accumulated spinal puncture was done practically as a routine measure on all infants admitted to the station. Bagley [3] has shown in experiments on puppies, in which small amounts of the pup's own blood were injected into the cerebrospinal fluid, the extremely irritating effect

3. Bagley, C., Jr.: Blood in Cerebrospinal Fluid, Resultant Functional and Organic Alterations in the Central Nervous System, Arch. Surg. **17**:18 (July) 1928.

of free blood, even in small amounts, in the circulating cerebrospinal fluid and pia-arachnoid meshwork. It is highly probable, in the light of Bagley's experiments, that when meningeal hemorrhage occurs that is not immediately fatal, if the bloody fluid is withdrawn by spinal puncture, recovery may occur. It is equally possible, and this happened in the aforementioned 7 cases, that the blood in the spinal fluid may disappear but the clotted blood beneath the pia-arachnoid and within the pia-arachnoid meshwork remains and by irritation causes death. It was noted that during the course of punctures done as a routine procedure not only did the general mortality from cerebral hemorrhage decrease but the general well-being of infants was improved. This is attributed to decreased cerebral irritation in these infants because of drawing off cerebrospinal fluid containing blood, which is present even in "normal" premature infants in microscopic amounts during the first days of life.

TABLE 3.—*Meningeal Hemorrhage or Acute Meningeal Congestion not Present at Necropsy**

	First Series		Second Series		Total	
	No. of Cases	Per centage	No. of Cases	Per centage	No. of Cases	Per centage
Spinal fluid grossly bloody or hazy	13	31	2	14	15	27
Spinal fluid clear	29	69	12	86	41	73

* Hazy fluids due to acute meningeal congestion were classified as faulty taps in the first series since no gross hemorrhage was present at necropsy.

Table 3 illustrates the frequency of bloody taps in both series in patients not suffering from meningeal hemorrhage as shown by necropsy. It will be noted that faulty taps occurred in 31 per cent of the first and in but 14 per cent of the second series. This is largely due to an appreciation of the fact that acute congestion of the meninges with microscopic hemorrhage is doubtless responsible for hazy cerebrospinal fluids when no gross hemorrhage has occurred. In the first series of seventy necropsies attention was directed to this condition by two cases in which, with extremely congested meninges, hazy cerebrospinal fluid occurred. The degree of congestion was so great it was considered remarkable that the cerebrospinal fluid was not grossly bloody. In the first series, such fluids, when gross meningeal hemorrhage was not present, were classified as being due to faulty taps.

In the second series of twenty-four necropsies, acute meningeal congestion was studied more closely and was found in five instances. The significance of this is twofold. First, 31 per cent of errors, or approximately one faulty tap out of three, is much too high a percentage of faulty punctures. Probably 14 per cent, as found in the second series, is nearer the correct percentage of error. It must be remembered that

this is with a technic of proved value in experienced hands. This definitely increases the diagnostic value of lumbar puncture in premature infants. Second, with the recognition of the relationship between acutely congested meninges and hazy spinal fluid, one must consider a new pathologic diagnosis, to be made on the basis of lumbar puncture. If one is reasonably certain of the technic and obtains a hazy fluid, one is justified in making a tentative diagnosis of acute meningeal congestion. Gross meningeal hemorrhage cannot possibly be ruled out, but when that occurs the cerebrospinal fluid is most frequently grossly bloody.

My previous report[3] on lumbar punctures in premature infants included a description of a benzidine test on the supernatant fluid obtained by centrifugation of bloody cerebrospinal fluid withdrawn by lumbar puncture. It was stated that if the puncture was performed with proper precautions to avoid hemolysis, the benzidine test was

TABLE 4.—*Relationship of the Age of the Premature Infant to the Icterus Index of the Cerebrospinal Fluid* *

Age in Days	Number of Cases	Average Icterus Index
1 or under	14	$\frac{5}{8}$
2 to 7	18	2
8 to 14	11	3
15 to 21	9	$1\frac{3}{8}$
22 to 28	12	1
29 to 49	11	$\frac{1}{2}$
49 or over	8	0

* Spinal fluid water-clear benzidine test negative, eighty-three fluids examined.

never positive in cases of accidental hemorrhage (i. e., that due to the trauma of the puncture), but was positive in 50 per cent of cases in which hemorrhage had occurred. It is not positive in 100 per cent of cases of meningeal hemorrhage, probably because the puncture is done before there is enough hemolysis to give a posititive benzidine test in the supernatant fluid. Shortly after this was reported, the same test was described by Schlack.[4] He stated, however, that if the benzidine test on the supernatant fluid is negative, meningeal hemorrhage can be ruled out. This is not true in my experience and for the reason stated. However, as far as my experience goes, if the test is positive it is definite proof that meningeal hemorrhage has occurred.

The relationship of the age of the premature infant to the degree of xanthochromia (icterus index) of the cerebrospinal fluid is shown in table 4. The benzidine test was done on the fluids to rule out the possibility that hemorrhage might have contributed to the color. The smallest infant in the series on whom lumbar puncture was performed

4. Schlack, H.: Beitrag zur diagnostischen Verwertbarkeit des blutigen Liquors, Munchen. med. Wchnschr. **75**:1502 (Aug. 31) 1928.

during life was ½ hour old and weighed 885 Gm. The youngest infant from whom a colorless spinal fluid was obtained was 35 days of age. This infant, according to the history, was only slightly premature (four weeks) and weighed 2,450 Gm. at birth. Another colorless fluid giving a negative benzidine reaction occurred in a patient aged 42 days with a clinical diagnosis of meningeal hemorrhage at the age of 4 days, when lumbar puncture had yielded a grossly bloody fluid. Very pale fluids, with a color detectable only on comparison with distilled water, may occur at any age after 7 days. It thus appears that xanthochromia is universally present in the cerebrospinal fluid of premature new-born infants.

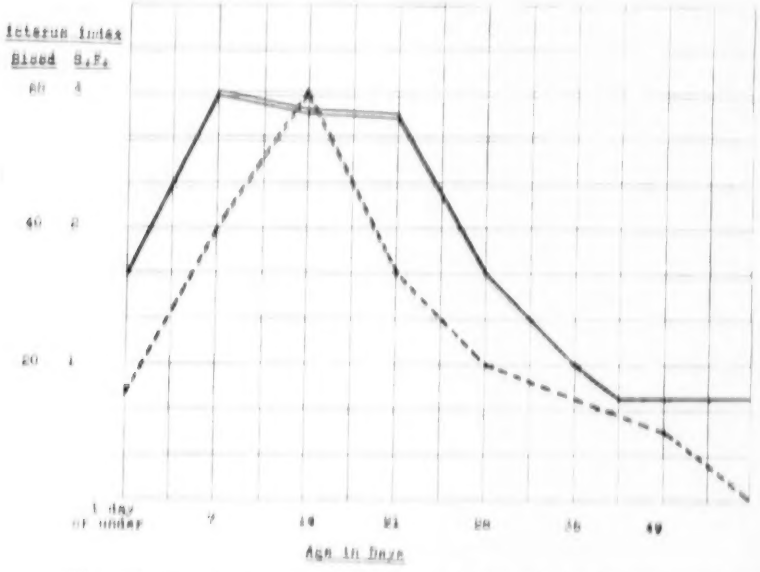
Two cases of nuclear (kern) icterus occurred in the entire series, both of them in the first series of 100 infants. The highest icterus index observed was 18. This occurred in an infant on whom puncture was performed only once, at the age of 52 days. The icterus index of the blood serum was 165 at this time. The clinical diagnosis was decomposition, secondary to meningeal hemorrhage, and icterus gravis, with possibly nuclear icterus. The necropsy diagnosis was icterus gravis and cerebral softening with no evidence of nuclear icterus. This serves to support the observation made previously [1] that icteric staining of the basal ganglions is not altogether dependent on the intensity of the yellow color of the cerebrospinal fluid or of the blood serum.

The indirect van den Bergh reaction was applied to sixty-six of the yellow cerebrospinal fluids of table 4. It was positive in thirty-six cases, or 55 per cent.

The direct van den Bergh reaction was negative in fifty-one of sixty-two determinations, or in 82 per cent of cases. Of the remaining eleven cases in which it was positive, three showed meningeal hemorrhage at necropsy, one presented icterus gravis with cerebral softening probably due to old hemorrhage, four patients survived and two died (no necropsy), in which cases meningeal hemorrhage had been diagnosed clinically, and the last patient was discharged alive with a clinical diagnosis of prematurity and pyelitis. This infant may have had meningeal hemorrhage without symptoms, as lumbar puncture was not done until the age of 32 days, by which time the red blood cells and hemoglobin would have disappeared from the spinal fluid. The evidence indicates that a positive direct van den Bergh reaction in the cerebrospinal fluid is suggestive of meningeal hemorrhage.

The relationship between the icterus index of the blood serum and the icterus index of the cerebrospinal fluid during the early weeks of life is illustrated graphically in the accompanying chart. The curves are plotted from the eighty-three cerebrospinal fluids of table 4 and the icterus index readings of seventy specimens of blood serum of premature infants. In many cases the blood specimens were obtained by

cardiac puncture immediately after death, but for a large part were obtained during life, by Dr. J. H. Hess and Dr. D. B. Witt [5] while making studies on the blood chemistry of premature infants. These curves may be taken as fairly representative for premature infants during the age period studied, since infants suffering from icterus in excess of that observed clinically under ordinary circumstances are not included. Of the blood serums, the series is made up of specimens obtained from twelve infants 1 day of age or less, fifteen infants from the remainder of the first week of life, seven from the second and third weeks of life, nine from the fourth and fifth weeks, eight from



The relationship between the icterus index of the blood serum and of the cerebrospinal fluid and the age of the premature infant. The broken line indicates the spinal fluid; the solid line, the blood serum.

the sixth week, four each from the seventh and eighth weeks and eleven infants after the eighth week of life.

These curves indicate that during the first six weeks of life the icterus index of the blood serum closely parallels the icterus index of the cerebrospinal fluid, the high points in both curves being reached during the second and third weeks of life, when the so-called physiologic icterus neonatorum is also most prominent. Roberts [6] has published curves for full-term infants similar in form but shorter in duration,

5. Hess, J. H., and Witt, D. B.: Unpublished work.

6. Roberts, M. H.: Relation of Pigment Content in Serum and Spinal Fluid of Newborn Infants, South. M. J. 31:460 (June) 1938.

since xanthochromia is usually absent from the cerebrospinal fluid of these infants after the ninth day of life.

From the parallel course of the curves of the accompanying chart it is practically impossible to escape the conclusion that there is a definite relationship between the icterus of blood serum and of cerebrospinal fluid during the early weeks of life. A detailed review of the literature regarding the relationship between icterus of blood and cerebrospinal fluid was included in the first report[1] of studies on cerebrospinal fluid in premature infants. Nothing since then has appeared in the literature which might change the conclusions reached in this review. These conclusions were that icterus ordinarily does not appear in the cerebrospinal fluid of adults unless there has been some damage to the choroid plexus or possibly the ependyma. If this is true, then the permeability of the blood-cerebrospinal fluid barrier of premature infants is probably associated with physiologic and histologic immaturity of the choroid plexus, which is generally recognized as the principal site of origin of the cerebrospinal fluid.[7]

A study of the literature regarding the microscopic structure of the choroid plexus indicates that the assumption mentioned may be correct. The histology of the choroid plexus has been investigated principally by Imamura,[8] Vonwiller[9] and von Zalka.[10] Definite changes in structure occur as age advances. Very early in life the epithelium is probably ciliated, as is the remainder of the lining of the neural canal. According to Vonwiller, this ciliation is present up to the time of birth when the cilia are lost. Von Zalka, however, was unable to demonstrate cilia in a 7 months embryo, although this may possibly have been due to differences in technic. In the new-born infant the epithelial cells are small and round and the cells of the plexus are practically not differentiated from the cells of the ependyma. Soon the cells of the plexus become larger and polygonal; vacuoles appear, together with granules, probably of a lipoid nature, and the cells suggest glandular epithelium. The villi of the plexus in the very young infant consist of capillary vessels with little connective tissue so that the epithelium of the plexus is directly adjacent to the capillary wall. The epithelial cells dominate the picture, the layer of cells being broader than that of the capillary vessels and connective tissue cells. The villi are long and their termina-

7. Weed, L. H.: The Cerebrospinal Fluid, Physiol. Rev. **2**:172, 1922.

8. Imamura, S.: Beiträge zur Histologie des Plexus choroideus des Menschen, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **8**:273, 1902.

9. Vonwiller, P.: Ueber das Epithel und die Geschwülste der Hirnkammern, Virchows Arch. f. path. Anat. **204**:330, 1911.

10. Von Zalka, E.: Beiträge zur Pathohistologies des Plexus choroideus: I. Die Altersveränderungen des Plexus choroideus, Virchows Arch. f. path. Anat. **207**:75, 1912.

tions show no expansions. As age advances the epithelial cells tend to flatten out. On the part of the connective tissue, diffuse and focal sclerosis occurs, and there are calcification, formation of psammoma, hyaline bodies and plexus cysts.

From the clinical side there is a certain amount of evidence of increased permeability of the blood-cerebrospinal fluid barrier in the very young infant. This is particularly true of circulating toxins, as in the meningismus of pneumonia. This, according to Rosenbaum,[11] is due to immaturity of the blood-cerebrospinal fluid barrier for a period after birth. Full-term infants show xanthochromia less often, and, when it is present, to a lesser degree than premature infants.[1] Segal and I,[12] in studying the cerebrospinal fluid in experimentally produced jaundice in adult and young dogs, did not find xanthochromia in adult dogs in which the icterus index of the blood serum was less than 150. In one case, in a dog a few weeks old, however, yellow spinal fluid was found when the icterus index of the blood serum was 28.

In the previous communication[1] it was pointed out that xanthochromia could, in part, be accounted for by pressure factors causing dilution of the cerebrospinal fluid with blood plasma at the time of birth during the process of labor. However, if xanthochromia is related to the immaturity of the infant, it might be expected that infants delivered by cesarean section would show xanthochromia. In the series here reported a spinal puncture was done on only one infant delivered by this method before labor began. The indication for the section was uremia. Gestation was of about thirty-three weeks, the birth weight was 1,895 Gm. and it was necessary to resuscitate the infant with oxygen and carbon dioxide. The spinal puncture was made three hours after birth; the cerebrospinal fluid was clear and slightly yellow with an icterus index less than 1. The infant died some hours afterward, and atelectasis and enlargement and edema of the thymus were found at necropsy. Garrahan,[13] working on full-term infants up to 17 days of age, found yellow cerebrospinal fluid in six of twelve infants delivered by cesarean section.

From the evidence quoted, it seems reasonable to assume that the close parallelism in intensity between the yellow color of the blood serum and the yellow color of the cerebrospinal fluid during the early weeks of life is due to immaturity, either anatomic or physiologic or both, of the blood-cerebrospinal fluid barrier.

---

11. Rosenbaum, S.: Die Permeabilität der Bluthirnschranke, Monatschr. f. Kinderh. **40**:303, 1928.

12. Segal, H. L., and Glaser, J.: Cerebrospinal and Ocular Fluids in Experimental Jaundice in Dogs, Arch. Path. **9**:1038 (May) 1930.

13. Garrahan, J. P.: La xantocromia fisiológica del liquido céfalorraquideo. Investigación en recién nacidos, Semana méd. **35**:123, 1928.

Roberts' studies[8] on full-term infants indicate that the average pigment ratio of cerebrospinal fluid to blood serum in normal infants is 1:125, while in cases of meningeal hemorrhage the ratio was 1:36. In his series the spinal fluid gave evidence of meningeal hemorrhage. In other words, the fluid was bloody, the readings being made on the supernatant fluid of centrifugated specimens of cerebrospinal fluid. However, if the spinal fluid is grossly bloody and one is reasonably certain of the technic, such a ratio is not needed as further evidence of the presence of meningeal hemorrhage, nor would such a ratio be of value if the fluid were bloody due to the trauma of the puncture. To be of value in attempting to diagnose meningeal hemorrhage purely on the basis of the degree of xanthochromia, one must know what the ratio will be when the cerebrospinal fluid is water-clear and the benzidine test negative. In eight infants on whom a lumbar puncture was made immediately after death and blood was withdrawn from the heart at the same time, the ratio of the icterus index of the cerebrospinal fluid to the icterus index of the blood serum was 1:22. Meningeal hemorrhage was not found in these infants at necropsy. In five cases in which meningeal hemorrhage was present at necropsy the ratio was 1:14. In each of the thirteen cases the cerebrospinal fluid was water-clear and xanthochromatic, and gave a negative benzidine reaction. The difference in the ratios is, of course, due to the transformation of the hemoglobin of the extravasated blood in the cerebrospinal fluid, in the cases of hemorrhage, into bilirubin and perhaps other pigments. The ratios are too close to be of any real diagnostic value, although perhaps a greater numerical difference might appear with a larger series. Possibly, also, there is not a greater difference between the ratios because the presumptive immaturity of the blood-cerebrospinal fluid barrier permits a certain freedom of passage of pigment between the blood and the cerebrospinal fluid in one direction, and between the cerebrospinal fluid and the blood in the other direction.

One of the most interesting of the clinical symptoms observed, which occasionally responded favorably to lumbar puncture, was the paroxysmal or intermittent cyanosis sometimes occurring in subtentorial hemorrhage. This type of cyanosis was mentioned in the first communication,[1] and was described later in more detail by Clein.[14] This symptom is characterized, as the name indicates, by periods of cyanosis that may be very intense, followed by periods of normal color or even marked redness of the skin. The cyanotic attacks may last from a few seconds to ten or fifteen minutes, and the intervals between the attacks are of practically the same length of time. Subtentorial hemorrhage is found at necropsy in these cases almost without exception. On

14. Clein, N. W.: Premature Infants, a Clinical and Pathologic Study, Am. J. Dis. Child. **37**:751 (April) 1929.

the basis of this symptom, together with the ruling out as far as possible of other causes of cyanosis, organizing circummedullary meningeal hemorrhage was diagnosed ante mortem in a full-term infant with normal cerebrospinal fluid at the age of 30 days.[15]

In patients presenting the type of cyanosis described, blood clots are found around the medulla oblongata at necropsy. The intermittent cyanosis, perhaps, may be explained on the basis of pressure by these clots affecting the respiratory or vasomotor centers, or both. Evidence in favor of this theory is found in certain facts brought out by the clinical and experimental observations of Cushing[16] in studies of the blood pressure in intracranial hemorrhage. His work indicates a regulatory mechanism which, under experimental conditions, is seemingly so adjusted that the vasomotor center tends to hold the arterial blood pressure within the medulla at a level slightly in excess of the extramedullary intracranial pressure which exerts a compressing force against the arterioles and capillary vessels situated in the medulla. In this way a fatal bulbar anemia, which would otherwise be the result of equalization of extramedullary and intramedullary tension, is avoided. Cushing pointed out that respiration is contingent on the efficiency of the vasomotor mechanism in holding the blood pressure at a certain level. Should the vasomotor mechanism fail to keep the arterial tension in the medulla above the extramedullary intracranial pressure, the respirations would cease immediately. Consequently, the sequence of events in cases of immoderate intracranial tension is primarily exhaustion of the vasomotor mechanism with a fall in blood pressure, and, secondarily, failure of respiration in consequence of the ensuing bulbar anemia.

Eyster,[17] in his work on the vasomotor and respiratory centers in relationship to Cheyne-Stokes' respiration, corroborated Cushing's observations and the general law formulated by him, namely, that "an increase of intracranial tension occasions a rise of blood pressure which tends to find a level slightly above that of the pressure exerted against the medulla." Eyster emphasized the fact that the medullary centers show marked differences in their reactions to anemia. The respiratory center is normally depressed by anemia while the vasomotor center is stimulated by this condition.

Although the mechanism of intermittent cyanosis is not definitely known, the sequence of events may be somewhat as follows: In sub-

15. Glaser, J.: Late Death as a Result of Cerebral Hemorrhage at Birth, Am. J. Dis. Child. **37**:807 (April) 1929.

16. Cushing, H.: The Blood-Pressure Reaction of Acute Cerebral Compression, Illustrated by Cases of Intracranial Hemorrhage, Am. J. M. Sc. **125**:1027, 1903.

17. Eyster, J. A. E.: Clinical and Experimental Observations upon Cheyne-Stokes Respirations, J. Exper. Med. **8**:565, 1906.

tentorial meningeal hemorrhage pressure is exerted, presumably, on the medulla oblongata by blood clots locally. To this may be added a general increase in intracranial tension secondary to interference with circulation of the cerebrospinal fluid by clots in the regions of the foramina of the fourth ventricle. As a result of this pressure there is an interference with the blood supply of the medulla oblongata, causing a certain degree of anemia. The vasomotor center, responding to the natural stimulus of anemia, causes an increase in blood pressure, and a consequently increased blood flow through the medulla oblongata, and a general increase of intracranial tension. Owing to pressure from without, the medulla is unable to respond to the increased blood flow by an increase in volume; congestion results; the internal pressure of the medulla is increased, and the circulation through it is diminished. The resulting anemia acts briefly as a stimulant and then as a depressant to the respiratory center; the respirations decrease, causing cyanosis, and finally the vasomotor center is exhausted due to interference with the nutritional supply of oxygen. Because of this the blood pressure drops, the congestion of the medulla is relieved, the respiratory center supplied with blood containing an excess of its normal stimulant, carbon dioxide, responds by increased respirations and the cyanosis disappears. Because of over-aeration of the blood the cyanosis may be succeeded by redness of the skin. This continues until the vasomotor center, again supplied with oxygenated blood, is able to bring up the blood pressure sufficiently to cause an increase in volume of the medulla oblongata with consequent interference with circulation. Naturally this is a vicious cycle that almost invariably ends in death unless the hemorrhage ceases and the excess bloody cerebrospinal fluid is withdrawn by lumbar puncture.

One case of meningitis occurred in the series. This was discovered accidentally during the course of a postmortem lumbar puncture done as a routine measure on a syphilitic infant of thirty-two weeks' gestation, who weighed 2,040 Gm. at birth and was 8 days of age at the time of death. The spinal fluid was greenish yellow and purulent and yielded a pure culture of pneumococcus type III. At the time of delivery, the mother of the infant was suffering from what was diagnosed as bronchopneumonia and from which she made an uneventful recovery. The necropsy diagnosis in this infant was congenital syphilis and primary pneumococcus meningitis. Pneumococcus meningitis of the full-term new-born infant has been previously described,[18] but not, as far as I can discover, in a prematurely new-born infant.

18. Heinz, H.: Pneumococcus Meningitis, New England J. Med. **199**:218 (Aug. 2) 1928. Uhr, J. S.: Pneumococcus Meningitis, Report of a Case in a Newborn Infant with Recovery, Arch. Pediat. **46**:121 (Feb.) 1929.

There was one death in this series which might possibly be attributable to spinal puncture. This was in an infant 23 days of age who had been tapped repeatedly because of a progressively increasing hydrocephalus, probably secondary to meningeal hemorrhage at birth. The infant died twenty-four hours after the last therapeutic drainage of cerebrospinal fluid. Permission for necropsy could not be obtained.

SUMMARY AND CONCLUSIONS

The observations previously reported on the cerebrospinal fluid of premature infants [1] have been largely corroborated.

Knowledge of the fact that hazy cerebrospinal fluid may be due to acute meningeal congestion permits a tentative diagnosis of this condition when hazy cerebrospinal fluid is obtained by lumbar puncture.

The recognition of this condition increases the diagnostic value of lumbar puncture and, in correlation with necropsy observations, has reduced the percentage of faulty taps to about 14 per cent.

Fifty-five per cent of the yellow cerebrospinal fluids of premature infants give a positive indirect van den Bergh reaction.

A positive direct van den Bergh reaction of the cerebrospinal fluid is suggestive of meningeal hemorrhage.

A positive benzidine test on the supernatant fluid after centrifugating bloody cerebrospinal fluid obtained by lumbar puncture with proper precautions to avoid hemolysis is proof of meningeal hemorrhage. If the test is negative, however, hemorrhage cannot be ruled out.

The highest icterus index of cerebrospinal fluid observed was 18 and occurred at the age of 52 days.

The youngest premature infant from whom a colorless cerebrospinal fluid was obtained was 43 days of age.

A case of primary pneumococcus meningitis is reported in a premature infant aged 8 days.

A theory is offered to explain the paroxysmal or intermittent cyanosis occurring in premature infants with subtentorial meningeal hemorrhage on the basis of intermittent pressure by blood clot on the medulla oblongata.

A chart is shown, illustrating the relationship between the icterus index of the blood serum and the icterus index of the cerebrospinal fluid. This curve reaches its peak during the second and third weeks of life.

Evidence is advanced in support of a theory that physiologic xanthochromia of the premature new-born infant, and probably of all new-born infants, occurs because of anatomic and physiologic immaturity of the blood-cerebrospinal fluid barrier.

233 Oxford Street.

SUSPECTED JUVENILE TUBERCULOSIS

EVALUATION OF CLINICAL SYMPTOMS AND SIGNS *

FREDERICK EBERSON, PH.D., M.D.

JESSIE P. DELPRAT, M.D.

AND

ERNST WOLFF, M.D.

SAN FRANCISCO

In an earlier publication one of us (F. E.)[1] studied 145 cases of juvenile tuberculosis with regard to history, symptomatology, physical and roentgenographic observations and tuberculin reactions. Reference was made to the need for analysis of the various symptom-complexes occurring among young patients and for the evaluation of symptoms and signs that might be considered important clinically. A subsequent analysis of 346 additional cases [2] indicated the value of correlating the numerous variables present in selected clinical groups of patients. This material had been classified in terms of exhaustive clinical data and comparative tuberculin tests. There remained, however, the important question regarding the significance of groups of symptoms and signs commonly observed in children, particularly among those suspected of having tuberculosis.

The present study was concerned with an attempt to evaluate the observations and to compare them singly and in combination, in terms of presumably significant clinical groupings. The method of approach to this problem was the same as that followed in our previous investigations. A complete clinical summary of each case was tabulated, and notation made of age, history of contact and previous diseases. The following symptoms were considered: repeated diseases of the upper part of the respiratory tract, cough, nervousness, lack of appetite, loss

* Submitted for publication, April 18, 1930.

* From the Department of Medicine, Department of Pediatrics and the George Williams Hooper Foundation for Medical Research, University of California Medical School, San Francisco.

Prof. Escholtzia Lucia and Miss Frances Russell of the Department of Vital Statistics and Biometry in the Department of Hygiene, and Miss Estelle Sturla, secretary, Department of Medicine, gave valuable assistance in the statistical study.

1. Eberson, F.: Am. Rev. Tuberc. **13**:124, 1926.

2. Eberson, F. and Wolff, E.: Clinical Study of Tuberculin Fractions Prepared from Nonprotein Culture Media, Am. Rev. Tuberc. **19**:327, 1929.

of weight or failure to gain, fatigability, night sweats, lassitude, and elevation of temperature. The physical signs, such as d'Espine's sign, paravertebral dulness, malnutrition, dulness of the manubrium sterni, enlargement of the cervical lymph nodes, abnormalities of percussion and auscultation, phlyctenular processes, involvement of bones and indications of tuberculous adenitis were recorded.

From roentgenographic studies the following data were tabulated: hilus calcifications, increased lung markings, enlargement of bronchial lymph nodes, calcification of bronchial lymph nodes, thickening of interlobar pleura, thickening of the apical pleura, peribronchial infiltration, primary focus and parenchymal tuberculosis.

TABLE 1.—*Showing the Comparative Number of Symptoms Observed in Group I with Positive Tuberculin Reactions and Group II with Negative Reactions*

Number of Symptoms in Individual Cases	Group I		Group II	
	Number	Per Cent	Number	Per Cent
None	75	36.4	42	42.0
One	34	16.5	21	21.0
Two	36	17.5	13	13.0
Three	33	16.0	10	10.0
Four	15	7.3	13	13.0
Five	9	4.4	..	....
Six	3	1.4	1	1.0
Seven	..	....	..	....
Eight	1	0.5	..	....
Total	206	100	100	100

Tuberculin tests were made simultaneously with ordinary human old tuberculin, toxic filtrate and alcohol-insoluble fraction for comparison.[3]

Two groups of children were selected on the basis of their reaction to tuberculin. The 206 giving positive reactions were segregated and classified as group I, while the 100 giving negative reactions were designated as group II. The distribution by age in both groups was practically the same, the maximum age being 17 years.

SYMPTOMS

It was found that in group I, 36.4 per cent (75 of the 206 cases) presented no symptoms, while in group II, 42 per cent (42 of the 100 cases) presented no symptoms (table 1). It was also found that in group I, approximately 16.5 per cent of the cases had one, two or three symptoms and 7.3 per cent had four, 4.4 per cent had five, and

3. Eberson, F.: Am. Rev. Tuberc. **13**:454, 1926; Proc. Soc. Exper. Biol. & Med. **24**:329, 331, 803, 1927; J. A. M. A. **90**:260 (Jan. 28) 1928.

1.4 per cent had six. In group II, 21 per cent had one symptom and approximately 11 per cent had two, three and four symptoms. These results show that one and four symptoms occurred more often among the cases in the negative group, while two, three, five and six symptoms in an individual occurred more often in the positive group.

These results are shown graphically in figure 1.

It was next determined how often a particular symptom occurred among the cases in the two groups alone and in combination with other

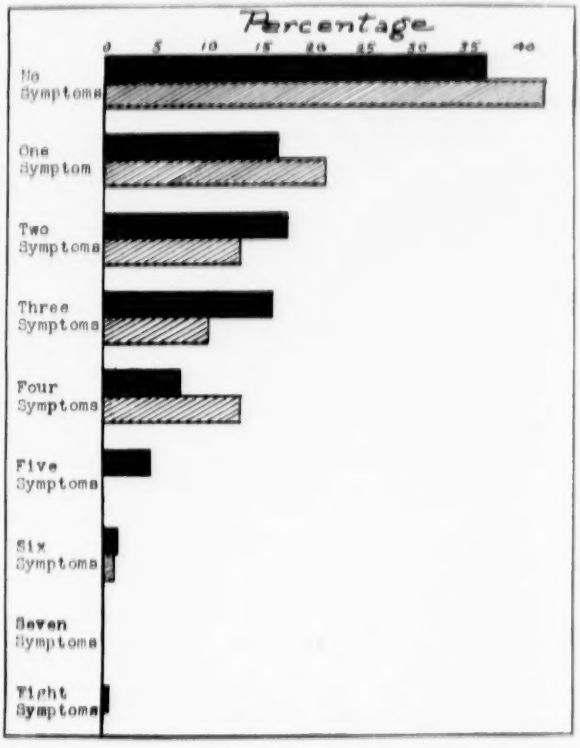


Fig. 1.—Number of symptoms in individual cases. Black columns indicate positive tuberculin reactions; columns of diagonal lines, negative.

symptoms. Nine symptoms were studied (table 2). The number in group I giving histories of one or more symptoms was 131 (63.6 per cent of 206). Among the 100 children with negative reactions (group II), 58 (58 per cent of 100) gave histories of one or more symptoms. The percentage distribution of the total number of cases in which symptoms occurred, alone or in combination with other symptoms, was based on the total number giving evidence of symptoms: that is, 131 in group I, and 58 in group II.

The symptoms that occurred the greatest number of times in both groups were cough (41.8 per cent in group I and 55.2 per cent in group II), and nervousness (41.8 per cent in group I and 39.6 per cent in group II). In group I these same symptoms occurred the greatest number of times alone and in combination with other symptoms; but in group II, cough, nervousness and fatigue occurred the greatest number of times alone, and cough, nervousness and lack of appetite occurred the greatest number of times when in combination with others.

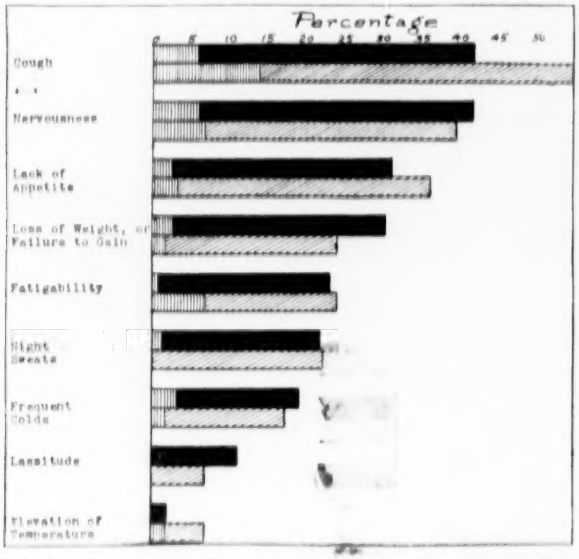


Fig. 2.—Relative frequency of various symptoms in total number of patients. Black columns indicate positive tuberculin reactions; diagonal lines, negative; columns of perpendicular lines, the occurrence of a particular symptom alone.

TABLE 2.—*Symptoms Listed in Descending Order of Occurrence in Group I*

	Total				Alone				With Others			
	Group I		Group II		Group I		Group II		Group I		Group II	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Cough	69	41.8	93	55.2	8	6.6	8	13.8	61	37.8	84	41.4
Nervousness	69	41.8	55	39.6	3	6.6	4	6.9	67	37.8	49	33.8
Lack of appetite	47	31.5	51	30.3	4	2.6	3	5.4	44	30.3	48	33.8
Loss of weight or failure to gain	46	30.6	14	24.1	4	2.6	1	1.7	43	27.6	13	22.4
Fatigability	39	25.5	14	24.1	1	0.7	4	6.9	34	23.6	10	17.2
Night sweats	33	21.6	13	22.4	3	1.8	...	...	31	20.6	13	22.4
Colds	30	19.3	10	17.2	3	3.3	1	1.7	24	16.6	9	15.5
Lassitude	17	11.3	4	6.9	...	...	...	...	17	11.3	4	6.9
Elevation of temperature	8	3.6	4	6.9	...	...	1	1.7	8	3.6	3	5.2

181 or 69.6 per cent of group I with symptoms.
58 or 58 per cent of group II with symptoms.

The differences between the percentages of total occurrences of symptoms in groups I and II were never found to be greater than 7 per cent, except in the case of cough, in which group II exceeded group I by 13.4 per cent. When considering symptoms occurring in combination with others, it was found that none exceeded a difference in percentage of 5.5 per cent, the greatest differences being in favor of group I in connection with loss of weight or failure to gain and nervousness.

Figures 2 and 3 are graphic representations of these facts.

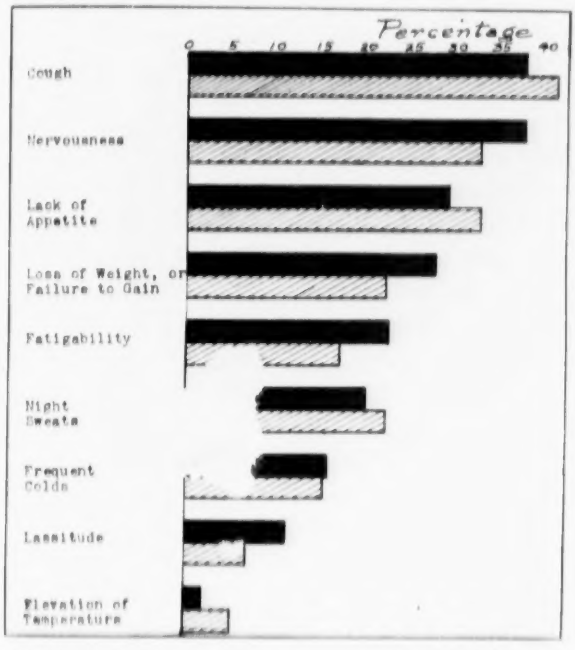


Fig. 3.—Relative frequency of various symptoms in combination with other symptoms. Black columns indicate positive tuberculin reactions; columns of diagonal lines, negative.

CLINICAL SYMPTOMS AND SIGNS

It was found that in group I, 11.2 per cent (23 of the 208 cases) and in group II, 12 per cent (12 of the 100 cases) presented no clinical observations in regard to tuberculosis (Table 5). Group I showed 6.8 per cent more cases in which one sign occurred; otherwise there were no appreciable differences in percentage. In both groups two signs occurred the greatest number of times (39 per cent in group II and 35 per cent in group I), and three signs were next in order (25 per cent in group II and 23.8 per cent in group I), group II exceeding group I in these instances.

These results are charted in figure 4.

The frequency of a particular clinical observation among the patients in the two groups was then determined. It was noted how often this observation occurred alone or in combination with others (table 4).

TABLE 3.—*Number of Clinical Symptoms and Signs in Individual Cases*

	Group I		Group II	
	Number	Per Cent	Number	Per Cent
None	23	11.2	12	12.0
One	48	23.3	17	17.0
Two	72	35.0	39	39.0
Three	49	23.8	25	25.0
Four	13	6.2	7	7.0
Five	1	0.5	...	...
Total	206	100.0	100	100.0

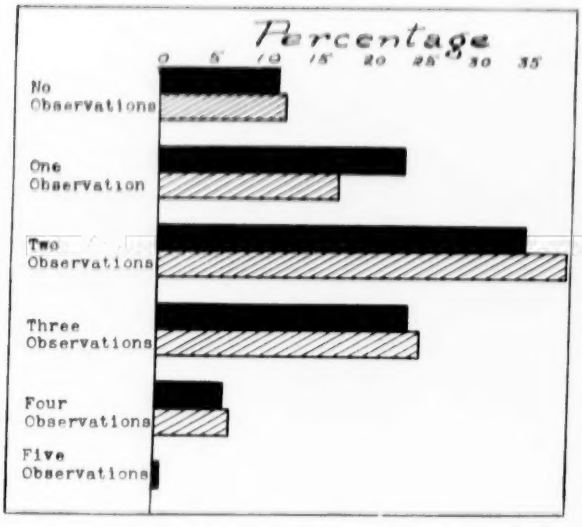


Fig. 4.—Number of clinical observations in individual cases. Black columns indicate positive tuberculin reactions; columns of diagonal lines, negative.

The number in group I giving histories of one or more clinical symptoms or signs was 183 (88.8 per cent of 206). Among the 100 children in group II, 88 (88 per cent of 100) gave histories of one or more observations. The percentage distribution of the total number of those cases in which clinical signs occurred alone or in combination with others was based on the total number giving evidence of clinical observations, that is, 183 in group I and 88 in group II.

Those clinical observations that occurred more often in group I than in group II were: malnutrition, dulness of the manubrium sterni, enlargement of the cervical lymph nodes and phlyctenular process; while d'Espine's sign, paravertebral dulness and auscultation observations exceeded in group II. The greatest difference was 20.1 per cent, which occurred in favor of group II in the case of paravertebral dulness, while the next greatest difference was found to be 10.4 per cent in favor of group I in the case of malnutrition.

The relative frequency of the different clinical signs and symptoms in the total number of patients is charted graphically in figure 5. The relative frequency of the same signs and symptoms when observed in combination with others is shown in figure 6.

TABLE 4.—*Clinical Observations Listed in Descending Order of Occurrence in Group I*

	Total				Alone				With Others			
	Group I		Group II		Group I		Group II		Group I		Group II	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
D'Espine's sign	150	82.0	78	88.6	27	14.8	11	12.5	123	67.2	67	76.1
Paravertebral dulness	111	60.6	71	80.7	7	3.8	5	5.7	104	56.8	66	75.0
Malnutrition	69	37.7	24	27.3	7	3.8	1	1.1	62	33.9	23	26.1
Manubrium sterni dulness	51	27.9	20	22.7	5	2.7	..	....	46	25.1	20	22.7
Cervical lymph nodes	7	3.8	1	1.1	2	1.1	..	....	5	2.7	1	1.1
Auscultation observations	6	3.3	3	3.4	..	....	..	....	6	3.3	3	3.4
Percussion observations	2	1.1	1	1.1	..	....	..	....	2	1.1	1	1.1
Phlyctenular process	2	1.1	..	....	..	....	..	....	2	1.1	..	....
Involvement of bone	...	....	..	....	..	....	..	....	...	....	..	....
Tuberculous adenitis	...	....	..	....	..	....	..	....	...	....	..	....

183 or 88.8 per cent of group I with clinical observations.
88 or 88.0 per cent of group II with clinical observations.

ROENTGENOGRAPHIC OBSERVATIONS

It was found that in group I, 5.8 per cent (12 of the 206 cases) presented no positive roentgen observations while in group II, 15 per cent (15 of the 100 cases) presented no such observations (table 5). A difference of 18.6 per cent in favor of group II presented one roentgen observation (57 per cent compared to 38.4 per cent); whereas 55.8 per cent showed two or more observations in group I, and only 28 per cent of group II showed two or more observations (fig. 7).

It was of interest to determine how often a particular roentgen observation occurred among the cases in the two groups, either alone or in combination with other observations. The nine roentgen observations were studied (table 6). The number of cases with histories of

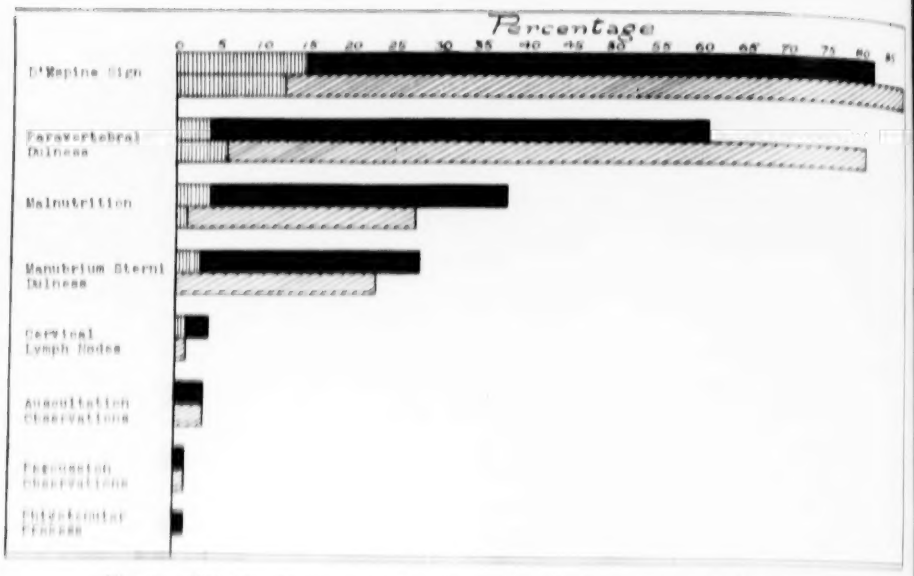


Fig. 5.—Relative frequency of various clinical observations in total number of patients. Black columns indicate positive tuberculin reactions; diagonal lines, negative; columns of perpendicular lines, the occurrence of a particular observation alone.

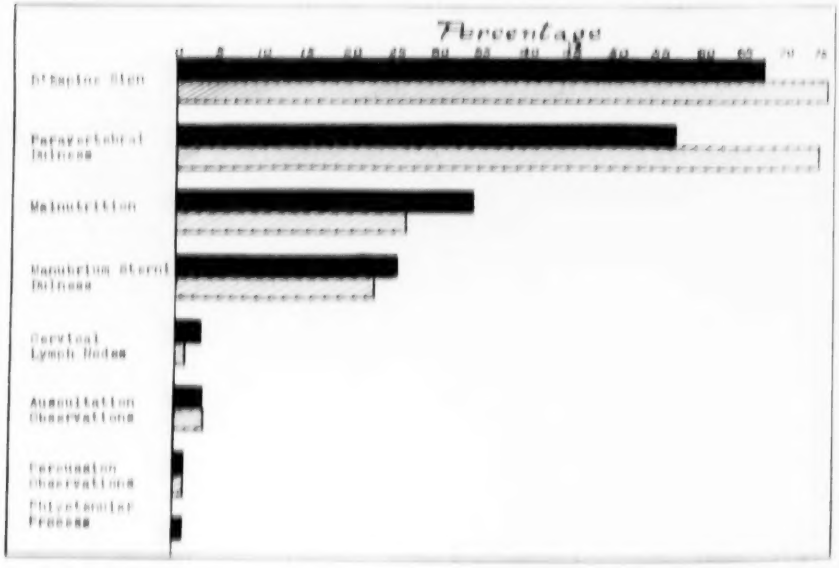


Fig. 6.—Relative frequency of clinical observations in combination with other clinical observations. Black columns indicate positive tuberculin reactions; columns of diagonal lines, negative.

one or more roentgen observation in group I totaled 194 (94.2 per cent of 206 cases). Among the 100 children with negative reactions (group II), 85 (85 per cent of 100 cases) gave histories of one or more roentgen observation. The percentage distribution of the total number of those cases in which roentgen observations occurred, alone or in combination with other observations, was based on the total number giving positive roentgen evidence, that is, 194 in group I and 85 in group II.

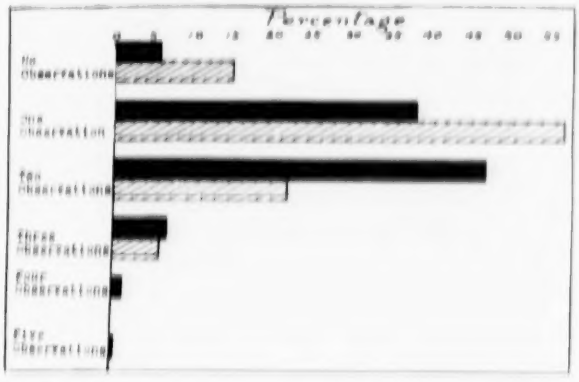


Fig. 7.—Number of roentgen observations in individual cases. Black columns indicate positive tuberculin reactions; columns of diagonal lines, negative.

TABLE 5.—*Showing Number of Roentgen Observations in Individual Cases*

Individual Cases	Group I		Group II	
		Per Cent		Per Cent
No observations	12	5.8	15	15.0
One observation	79	38.4	57	57.0
Two observations	97	47.1	33	33.0
Three observations	14	6.8	0	0.0
Four observations	3	1.4		
Five observations	1	0.5		
Total	206	100.0	100	100.0

194 or 94.2 per cent of group I with roentgen ray observations.
85 or 85.0 per cent of group II with roentgen ray observations.

The roentgen evidence that occurred more often in group I than in group II was: hilus calcifications, increased markings and thickened interlobar pleura. Peribronchial infiltration was found to occur more often in group II than in group I, and the remainder of the roentgen observations occurred approximately the same percentage of times in both groups.

When the roentgen evidence was considered as it occurred in combination with other roentgen evidence in the same person, group I

exceeded group II in every instance. However, when only one observation occurred in the person, group II exceeded group I in every case, particularly hilus calcifications, increased markings, enlarged bronchial lymph nodes and peribronchial infiltration.

The relative frequency of certain roentgen evidence in the total number of patients, with reference to the occurrence of this evidence alone or in combination with other observations, is strikingly illustrated in figures 8 and 9.

As an aid in diagnosis, the roentgen observations presented the most favorable picture with regard to differences between the two

TABLE 6.—*Roentgen Observations Listed in Descending Order of Occurrence in Group I*

Observations	Total				Alone				With Others			
	I		II		I		II		I		II	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Hilus calcifications	120	61.8	39	45.9	38	19.6	21	24.7	82	42.2	18	21.2
Increased markings	78	40.3	27	31.8	10	5.2	10	11.8	68	35.1	17	20.0
Enlarged bronchial lymph nodes	61	31.4	26	30.6	20	10.2	14	14.1	41	21.2	12	16.5
Thickened interlobar pleura	35	18.1	9	10.6	5	2.6	3	3.5	30	15.5	6	7.1
Peribronchial infiltration	22	11.4	14	16.5	3	1.5	6	7.1	19	9.9	8	9.4
Calcified bronchial lymph nodes	7	3.6	3	3.5	2	1.0	2	1.2	5	2.6	1	2.3
Primary focus	7	3.6	1	1.2	1	0.5	1	1.2	6	3.1	..	1.2
Thickened apical pleura	2	1.0	..	....	..	....	..	....	2	1.0	..	....
Parenchymal tuberculosis	..	....	..	....	..	....	..	....	..	....	..	....

groups with positive and negative reactions to tuberculin. A study of these observations, however, indicated that no such differences existed between these two groups of patients in relation to distribution of symptoms and clinical signs in terms of the more important roentgen observations (tables 7 and 8, figure 10). Reference to tables 2 and 4 will show that the frequency of symptoms (in descending order of occurrence) could not be demonstrated. The clinical observations, however, maintained their relative order of occurrence with respect to D'Espine's sign, paravertebral dulness, malnutrition and dulness of the manubrium sterni. By comparing these observations further in the two groups of persons with positive and negative tuberculin reactions it could be seen at a glance that the outstanding physical signs and symptoms were much more prevalent in the negative group! Indeed,

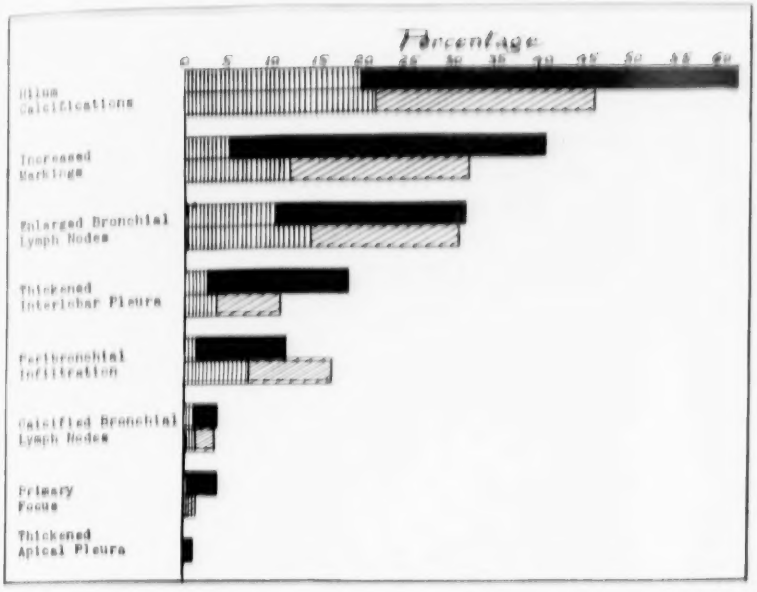


Fig. 8.—Relative frequency of roentgen observations in total number of patients. Black columns indicate positive tuberculin reactions; columns of diagonal lines, negative; perpendicular lines, the occurrence of a particular observation alone.

Fig. 9.—Relative frequency of roentgen observations in combination with other roentgen observations. Black columns indicate positive tuberculin reactions; columns of diagonal lines, negative.

TABLE 7.—*Study of the Roentgen Evidence in Relation to Symptoms and Clinical Signs in Persons with Positive (Group I) and Negative (Group II) Reactions*

Roentgenographic observations	Persons Presenting 3 or More Symptoms				Persons Presenting 3 or More Clinical Observations			
	Persons with Positive Reactions		Persons with Negative Reactions		Persons with Positive Reactions		Persons with Negative Reactions	
	N = 180 Cases	N. %	N = 90 Cases	N. %	N = 180 Cases	N. %	N = 90 Cases	N. %
Minimal calcification	No symptoms 40 22 Nervousness 39 22 Loss of weight 38 21 Cough 33 18 Lack of appetite 33 18 Fatigability 33 18 Night sweats 32 18 Lassitude 12 7 Colds 11 6 Fever 2 1		No symptoms 15 17 Nervousness 14 16 Cough 9 10 Lack of appetite 8 9 Loss of weight 4 4 Night sweats 4 4 Colds 5 6 Fatigability 5 6 Fever 1 1		D'Espine sign 69 38 Vertebral dullness 64 36 Malnutrition 40 22 Manubrium sterni 39 22 No clinical signs 13 7 Auscultation observations 4 2 Cervical lymph nodes 3 2 Percussion observations 3 2 Phlyctenular process 1 1		D'Espine sign 30 33 Vertebral dullness 23 26 Malnutrition 12 13 Manubrium sterni 9 10 Auscultation observations 4 4 Cervical lymph nodes 1 1	
Increased lung markings	N = 78 Cases		N = 27 Cases		N = 78 Cases		N = 27 Cases	
	No symptoms 31 40 Nervousness 22 28 Cough 18 23 Loss of weight 17 22 Night sweats 14 18 Fatigability 13 17 Lack of appetite 12 15 Colds 6 8 Lassitude 3 4 Fever 1 1		Cough 10 37 No symptoms 9 33 Lack of appetite 8 30 Nervousness 5 18 Night sweats 4 15 Colds 4 15 Loss of weight 3 11 Lassitude 3 11 Fatigability 1 4 Fever 1 4		D'Espine sign 55 70 Vertebral dullness 42 54 Malnutrition 14 18 Manubrium sterni 14 18 No clinical signs 11 14 Cervical lymph nodes 5 6 Auscultation observations 3 3 Percussion observations 1 1 Phlyctenular process 1 1		Vertebral dullness 23 85 D'Espine sign 21 78 Malnutrition 6 22 Manubrium sterni 6 22 No clinical signs 3 11 Auscultation observations 2 7	
Enlarged bronchial lymph nodes	N = 61 Cases		N = 30 Cases		N = 61 Cases		N = 30 Cases	
	Cough 54 90 Nervousness 18 30 No symptoms 17 28 Colds 16 24 Loss of weight 15 25 Lack of appetite 15 25 Night sweats 15 25 Fatigability 10 16 Lassitude 6 8		No symptoms 10 33 Cough 7 23 Lack of appetite 6 20 Nervousness 6 20 Night sweats 4 13 Loss of weight 3 12 Fatigability 3 12 Colds 3 12 Lassitude 1 4 Fever 1 4		D'Espine sign 40 73 Vertebral dullness 22 40 Malnutrition 24 39 Manubrium sterni 20 33 No clinical signs 7 11 Cervical lymph nodes 2 3 Phlyctenular process 1 2 Auscultation observations 1 2		D'Espine sign 21 21 Vertebral dullness 10 33 Malnutrition 3 10 Manubrium sterni 4 13 No clinical signs 3 10 Cervical lymph nodes 2 7 Auscultation observations 1 4	
Thickened interlobar pleura	N = 35 Cases		N = 9 Cases		N = 35 Cases		N = 9 Cases	
	Cough 14 40 Nervousness 12 34 Lack of appetite 9 26 Fatigability 9 26 No symptoms 8 23 Loss of weight 6 17 Night sweats 6 17 Colds 6 17 Lassitude 4 11 Fever 1 3		Cough 4 44 Colds 3 33 No symptoms 3 33 Lack of appetite 1 11 Nervousness 1 11		D'Espine sign 20 57 Vertebral dullness 19 54 Manubrium sterni 12 34 Malnutrition 10 28 No clinical signs 4 11 Phlyctenular process 2 6 Percussion observations 1 3 Auscultation observations 1 3 Cervical lymph nodes 1 3		D'Espine sign 7 78 Vertebral dullness 7 78 Manubrium sterni 3 33 Malnutrition 2 22 No clinical signs 1 11	

TABLE 7.—*Study of the Roentgen Evidence in Relation to Symptoms and Clinical Signs in Persons with Positive (Group I) and Negative (Group II) Reactions—Continued*

Roentgen observations	Persons Presenting 3 or More Symptoms				Persons Presenting 3 or More Clinical Observations			
	Persons with Positive Reactions		Persons with Negative Reactions		Persons with Positive Reactions		Persons with Negative Reactions	
	N = 99 Cases	%	N = 14 Cases	%	N = 99 Cases	%	N = 14 Cases	%
Peribronchial thickening	Lack of appetite	7 33	Cough	6 43	D'Espine sign	15 60	D'Espine sign	13 93
	Cough	7 33	Lack of appetite	5 36	Vertebral dullness	11 50	Vertebral dullness	7 50
	No symptoms	6 27	Nervousness	4 29	Malnutrition	9 39	Malnutrition	4 29
	Loss of weight	5 23	Colds	4 29	Manubrium sterni	4 15	Manubrium sterni	3 14
	Nervousness	5 23	Loss of weight	3 21	No clinical signs	4 15	No clinical signs	3 14
	Colds	4 18	Night sweats	3 21	Cervical lymph nodes	4 4		
	Night sweats	3 0	No symptoms	3 21				
	Fatigability	1 4	Fatigability	2 14				
	Lassitude	1 4	Lassitude	1 7				
	Fever	1 4	Fever	1 7				
Calcified tracheobronchial lymph nodes	N = 7 Cases		N = 3 Cases		N = 7 Cases		N = 3 Cases	
	No symptoms	3 ..	Loss of weight	1 ..	Vertebral dullness	4 ..	D'Espine sign	2 ..
	Fatigability	2 ..	Lack of appetite	1 ..	D'Espine sign	3 ..	Vertebral dullness	2 ..
	Nervousness	2 ..	Cough	1 ..	Manubrium sterni	3 ..	No clinical signs	1 ..
	Loss of weight	1 ..	Night sweats	1 ..	Malnutrition	2 ..		
	Night sweats	1 ..	Colds	1 ..	Phlyctenular process	1 ..		
	Fever	1 ..	No symptoms	1 ..	No clinical signs	1 ..		
	Colds	1 ..						
Primary focus	N = 7 Cases		N = 1 Case		N = 7 Cases		N = 1 Case	
	Nervousness	3 ..	No symptoms	1 ..	D'Espine sign	6 ..	D'Espine sign	1 ..
	Loss of weight	2 ..			Vertebral dullness	5 ..	Vertebral dullness	1 ..
	Lack of appetite	2 ..			Malnutrition	3 ..		
	No symptoms	2 ..			Manubrium sterni	1 ..		
	Fatigability	1 ..						
	Cough	1 ..						
	Fever	1 ..						
Thickened pleura	N = 4 Cases				N = 4 Cases			
	Lack of appetite	3 ..			D'Espine sign	3 ..		
	Fatigability	1 ..			Malnutrition	3 ..		
	Cough	1 ..			Vertebral dullness	3 ..		
	Night sweats	1 ..						
	Nervousness	1 ..						
	No symptoms	1 ..						

this correlation was striking enough to warrant the deduction that the stated observations were probably characteristic of nontuberculous processes in the lung. With regard to the presented symptoms and the particular roentgen evidence, it was found that such correlation as was apparent had no bearing on the question of whether or not tuberculosis existed. An exception to this was seen in connection with the roentgen evidence of thickened interlobar pleura (table 8); but even in this instance there was no difference between the positive and negative tuberculin groups with regard to the clinical observations.

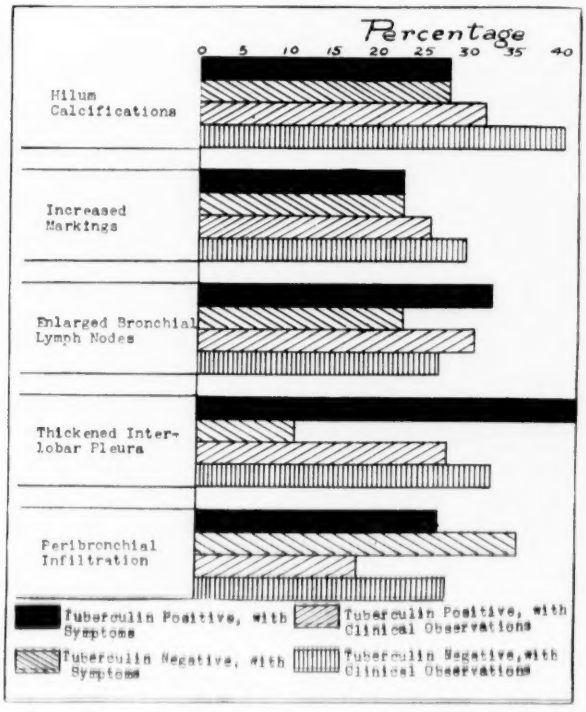


Fig. 10.—Comparison of roentgen observations in patients with three or more symptoms or clinical signs.

TABLE 8.—*Number and Percentage of Persons with Positive and Negative Reactions with Certain Roentgen Evidence Who Gave Histories of Having Three or More Symptoms or Clinical Signs*

	Symptoms				Clinical Observations			
	(Positive)		(Negative)		(Positive)		(Negative)	
	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
Hilus calcification	91	98	11	92	98	97	10	91
Increased markings	48	94	6	86	90	96	3	90
Enlarged bronchial lymph nodes	30	94	6	86	30	91	7	87
Thickened interlobar pleura	13	81	4	67	30	94	2	67
Peribronchial infiltration	9	75	3	50	4	80	1	50
Calcified bronchial lymph nodes	1	33	0	00	3	60		
Primary focus	0	00	0	00	1	100		
Thickened apical pleura	2	67	0	00	2	67		

COMMENT

This study has brought out the important fact that there was little or no difference between a group with positive and a group with negative tuberculin reactions, as judged by nine symptoms and ten clinical signs under consideration. The greatest differences between the two groups

seemed to be in terms of the nine roentgen observations that were studied. The evidence presented showed that the commonly accepted clinical symptoms and signs have no diagnostic significance, except as they may be correlated with roentgenograms and the tuberculin test when these are definitely positive for tuberculosis. As a diagnostic criterion roentgenograms in conjunction with the tuberculin test were unquestionably of diagnostic value. Certain roentgen observations occurring alone appeared to have no critical value for diagnosis, although such observations have been considered in the past as definitely pathognomonic.

The data presented an excellent picture of what might be expected from purely chance fluctuations. There was no selective sampling by dividing the groups into positive and negative reactors. It was realized that in a study of this kind statistical evaluation becomes more and more difficult, as the groups become too small by continued subdivision.

With reference to the newer interpretation of roentgen evidence emphasized by McPhedran,[4] Armand-Delille,[5] Hawes and Friedman[6] and others, it is now clear that the terms "hilus calcification," "increased bronchial markings," "enlarged lymph nodes," and "primary focus" have been inadequately defined and interpreted differently by different observers. According to McPhedran, calcification of the lymph nodes can be recognized only as shadows having a granular appearance. Furthermore, the increase of perihilar shadows is due, not to enlargement of bronchial lymph nodes, but to the pulsation and vibration of the arteries, giving an appearance that has been interpreted erroneously.

An analysis by Wolff and Stone[7] of a series of negative tuberculin reactors has emphasized the significance of interpreting x-ray films in the light of McPhedran's criteria. In their study, which was a preliminary review of some of the data now presented in this complete present report, it was concluded that a diagnosis of tuberculosis could not be based on the observations of localized increased markings of the lungs or of the axial shadows. They found no calcifications, no enlargement of lymph nodes and no localized pulmonary infiltrations.

In terms of these more modern concepts, an explanation is found for the infrequent pathologic evidence of tuberculosis at autopsy as compared with the diagnosis made on the basis of roentgenograms of the chest.[8] It is significant also, from our study, that interpretations of

4. McPhedran, F. M.: Am. J. M. Sc. **173**:313, 1927.

5. Armand-Delille, P. F., and Lestocquoy, C.: The Diagnosis of Tuberculosis of the Tracheobronchial Gland, Am. J. Dis. Child. **38**:1125 (Dec.) 1929.

6. Hawes, J. B., and Friedman, E.: Interpretation of Roentgenograms in Tracheobronchial Gland Tuberculosis, J. A. M. A. **92**:609 (Feb. 23) 1929.

7. Wolff, E., and Stone, R. S.: J. A. M. A. **94**:458 (Feb. 15) 1930.

8. Bigler, J. A.: Interpretation of Roentgenograms of the Chest in Children Based on Observations of Necropsy: II: Tuberculosis, Am. J. Dis. Child. **38**:1166 (Dec.) 1929.

roentgen evidence must depend not only on the occurrence of individual roentgen observations, but on their occurrence in combination with others. These facts are demonstrated conclusively in tables 6, 7 and 8.

It was interesting to observe the remarkable correlation between certain roentgen observations and physical signs, such as dulness of the manubrium sterni and paravertebral areas and D'Espine's sign. These observations, however, were not related to the presence of tuberculosis, and indicated in the striking manner the fallacy of drawing conclusions from physical observations and clinical symptoms without careful roentgen studies and the tuberculin test.

SUMMARY AND CONCLUSIONS

A clinical and roentgen study of 306 cases of suspected juvenile tuberculosis has been made with special reference to the evaluation of nine clinical symptoms ten clinical signs nine roentgen observations and the tuberculin test. The data were subjected to exhaustive statistical analysis.

Two groups of children were selected on the basis of their reaction to tuberculin. It was found that in the positive group (206 patients), 36.4 per cent presented no symptoms as compared with 42 per cent among the negative reactors (100 patients). One and four symptoms occurred more often among the cases in the negative group, while two, three, five and six symptoms occurred more often in the positive group.

The symptoms that occurred most often in both groups were cough (41.8 per cent among the positive, and 55.2 per cent among those with negative reactions); and nervousness (41.8 per cent among the positive, and 39.6 per cent among those with negative reactions).

The differences between the percentages of total occurrences of symptoms in both groups were never greater than 7 per cent, except in the case of cough, which in the series of persons with negative reactions exceeded those with positive reactions by 13.4 per cent.

Considering symptoms occurring in combination with others, it was found that none exceeded a difference in percentage of 5.5 per cent, the greatest differences being in favor of the persons with positive reactions in connection with loss of weight or failure to gain and nervousness.

It was found that in the tuberculin-positive group 11.2 per cent, and in the tuberculin-negative group 12 per cent, presented no clinical observations. One sign occurred 6.3 per cent more often in the positive group; but otherwise there were no appreciable differences in percentage. Two observations occurred most frequently in both groups (39 per cent among those with negative, and 35 per cent among those with positive, reactions). Three observations were next in order (25 per cent in the negative, and 23.8 per cent in the positive group). In all these instances the negative exceeded the positive group.

The percentage of patients in the positive group giving histories of one or more clinical symptoms or signs was 88.8, and in the negative group, 88.

The percentage distribution of the total number of cases in which a clinical symptom or sign occurred alone or in combination with others was as follows: In the positive group, malnutrition, dulness of the manubrium sterni and enlargement of the cervical lymph nodes occurred more often; while D'Espine's sign, paravertebral dulness, and auscultation exceeded among those with negative reactions. The greatest difference of 20.1 per cent occurred in favor of the negative group in the case of paravertebral dulness. The next greatest difference was 10.4 per cent in favor of the positive group in the case of malnutrition.

It was found that in the positive group 5.8 per cent, and in the negative group 15 per cent presented no roentgen evidence. One roentgen observation occurred in 57 per cent of those with negative and in 38.4 per cent of those with positive reactions; and 55.8 per cent in the positive group showed two or more observations as compared with 28 per cent in the negative group.

The percentage giving histories of one or more roentgen observations was 94.2 per cent in the positive and 85 per cent in the negative group.

The percentage distribution of the total number of cases in which roentgenographic signs occurred alone or in combination with others was as follows: In the positive group, hilus calcifications, increased bronchial markings and thickened interlobar pleura occurred more often; in the negative group, peribronchial infiltration occurred more frequently; and the remainder of the roentgenographic signs occurred approximately in the same percentage in both groups.

Considering the roentgen observations as they occurred in combination with other evidence in the same individual, those with positive reactions exceeded the negative group in every instance. When only one observation occurred, such as hilus calcifications, increased bronchial markings, enlarged bronchial lymph odes or peribronchial infiltration, the negative group exceeded the positive in every case.

The analysis indicated the importance of comparing roentgen data not only with respect to their occurrence in two groups of patients, but with regard to distribution of all the factors studied.

Roentgen observations presented the most favorable picture regarding differences between groups with positive reactions to tuberculin and those with negative reactions. However, in relation to the distribution of symptoms and clinical signs, in terms of the more important roentgen evidence, such differences did not exist.

Certain outstanding physical evidence, such as D'Espine's sign, paravertebral dulness, etc., was more prevalent among persons with negative tuberculin reactions. Observations that have been considered in the

past as pathognomonic of tuberculosis were associated with nontuberculous processes in the lung. Such roentgen evidence, occurring alone, appeared to have no diagnostic value.

Evidence that has been presented in this study showed that commonly accepted clinical symptoms and signs have no diagnostic significance unless these are definitely correlated with positive tuberculin tests and roentgen observations that are positive for tuberculosis.

The data in the report presented an excellent picture of what might be expected from purely chance fluctuations. There was no selective sampling by dividing the groups of patients into those with positive and those with negative reactions.

The newer interpretation of roentgen observations suggested by McPhedran and others has been emphasized by our own observations. In terms of these more modern concepts an explanation has been found for the infrequent pathologic evidence of tuberculosis at autopsy as compared with the diagnoses on the basis of x-ray films of the chest.

It is believed that the use of tuberculin fractions such as we have described in earlier work have proved their superiority to ordinary tuberculins, as this clinical and rigorous biometric analysis has again demonstrated.

STUDIES IN IMMUNITY

II. THE EFFECT ON THE SKIN TUBERCULIN REACTION OF NONSPECIFIC FACTORS *

BERNICE EDDY, PH.D.
AND
A. GRAEME MITCHELL, M.D.
CINCINNATI

In a previous communication, we [1] attempted to give partial answers to two questions: 1. Is a positive skin reaction to tuberculin an absolute indication of tuberculous infection? 2. Is there ever absence of the tuberculin skin reaction in patients infected with the tubercle bacillus?

From a review of the literature and our own studies, certain conclusions were reached which may be stated briefly as follows: A positive reaction of the skin to tuberculin is approximately two to four times as frequent during the convalescent afebrile stage as during the acute stage of such diseases as measles, diphtheria, scarlet fever, varicella, poliomyelitis, pneumonia, influenza, gastro-enteritis, etc. There is some evidence that larger doses of tuberculin may cause a positive skin reaction to occur during the febrile stage of these diseases. Readings of skin tuberculin reactions during acute diseases should be continued for several days, as the skin response may be delayed longer than forty-eight hours.

The observations have been continued and elaborated, and the present report is not only a record of them, but it is also an effort to answer other questions which naturally came to mind during the study. The personal equation was obviated as much as possible by having the tests and readings performed by one person (B. E.) whose entire time was devoted to this particular study for a period of about two years. It was necessary to perform 5,000 tests in order to secure records on approximately 1,000 patients who were studied during both the acute and the convalescent stages of disease, and to attempt to gather data on well children whom we might observe later if they became acutely ill. The patients were children admitted to the pediatric and contagious wards of the Cincinnati General Hospital. The criteria for conva-

* Submitted for publication, April 19, 1930.

* From the B. K. Rachford Department of Pediatrics of the College of Medicine of the University of Cincinnati.

1. Mitchell, A. G.; Wherry, W. B.; Eddy, Bernice, and Stevenson, E. E.: Studies in Immunity; Nonspecific Factors Influencing Reaction of Skin to Tuberculin, Am. J. Dis. Child. **36**:720 (Oct.) 1928.

lescence were the usual ones, such as length of time after onset, absence of fever and complications, etc. None of the patients was tested later than thirty-five days after the onset of the acute disease. The material used was Koch's old tuberculin which had been carefully standardized; it was injected intracutaneously, and the dose was contained in 0.1 cc. of a solution of 0.85 per cent sodium chloride to which 0.5 per cent phenol had been added as a preservative. Bovine tuberculin was employed in doses of 0.01 mg. and human tuberculin in doses of 0.01, 0.1 and 1 mg. Readings were made at daily intervals for a week and often for longer. For the present purpose, only those skin reactions were considered positive, which at the end of forty-eight hours had an erythema at least 1 cm. in diameter and which were accompanied by elevation of the skin. Only active tuberculin, proved so by skin tests on known positive reactors, was employed. One hundred and ninety-six control tests were made with glycerinated broth evaporated and diluted with a solution of 0.85

TABLE 1.—*Tuberculin Test During Acute and Convalescent Stages of Disease in the Same Patients*

Disease	Number of Cases	Febrile Stage		Convalescent Stage	
		Number Positive	Per Cent Positive	Number Positive	Per Cent Positive
Measles	200	7	3.5	30	15.0
Diphtheria	105	13	12.0	91	86.0
Poliomyelitis	38	3	8.0	4	10.5
Scarlet fever	435	17	4.0	84	19.0
Varicella	52	4	8.0	13	25.0
Pertussis	75	3	4.0	3	4.0
Miscellaneous	42	2	6.0	5	16.0
Total	934	49	5.0	150	17.0

per cent sodium chloride containing 0.5 per cent phenol. Only three of these tests caused an erythema with a diameter as great as 1 cm., and this was not accompanied by swelling of the skin.

In table 1 is shown the comparison of tuberculin skin reactions during the acute febrile stage and the convalescent afebrile stage of several diseases. There is not itemized the type of tuberculin (bovine or human) or the dosage employed, but it was always similar in the same patient. Thus, if 0.01 mg. of bovine tuberculin was injected during the febrile stage of a disease, the same material and dosage was employed during convalescence in the same patient. According to the figures a greater number of positive reactions was obtained during convalescence than during the acute stage in all diseases except pertussis; in poliomyelitis there was practically no difference. If all the diseases are considered together, the number of positive tuberculin reactions is found to be more than three times greater during convalescence than during the acute stage. The forty-nine patients who had positive reactions during the acute stage, all had positive ones also during convalescence.

The question immediately arises concerning the skin response of these children before the onset of the acute disease. Several hundred tuberculin tests were performed on children who were inmates of orphan asylums and children's homes from which patients, when acutely ill, were sent into the wards of the Cincinnati General Hospital. Only eighty-eight of these were admitted within six months following their initial test.

The number of cases given in table 2 is not large enough to permit any definite conclusion. It is interesting and perhaps significant that the number of positive tuberculin skin tests is about three times greater before the onset of the acute disease than during the early stage of it.

We have considered the possibility that there is a depression but not an absence of skin response to tuberculin during the acute febrile stage of these diseases. This could be determined by varying the dosage. In twenty-nine patients we obtained, during the acute stage

TABLE 2.—*Tuberculin Tests Before and During Acute Diseases*

Disease	Number of Cases	Prior to Disease		Febrile Stage, Acute Illness	
		Number Positive	Per Cent Positive	Number Positive	Per Cent Positive
Measles	20	6		1	
Diphtheria	12	1		1	
Scarlet fever	11	1		0	
Varicella	22	0		2	
Pertussis	18	2		1	
Miscellaneous	5	0		0	
Total	88	10	18.0	5	5.7

of a disease, positive results in tests with doses of 0.1 or 1 mg. of tuberculin but negative results in tests with 0.01 mg. During convalescence in these same patients, a smaller dose than that employed earlier produced a positive skin reaction. Fourteen patients, too, in whom 1 or 0.1 mg. did not produce a positive result in a test during the acute stage, did react during convalescence to doses of 0.01 mg. In this same connection, the size of the skin reaction might be of significance. Twenty-three of the forty-nine patients who had a positive test both during the acute phase of the disease and during convalescence had a skin reaction of greater diameter at the later injection with the same amount of tuberculin. The reverse of this, namely, greater reactions during the acute stage than during convalescence, was not true in any instance. We may attach some importance to this because of the fact that the amount of tuberculin was accurately standardized and that the attempt was made always to inject the same amount of solution in comparative tests. This increase in the size of the reaction during convalescence varied from one-half to three times that of the skin erythema during the acute stage.

In twenty-seven patients, the skin response to tuberculin was delayed longer than forty-eight hours. This is shown in table 3. The significance of this delay in skin response is not clear. Twelve of the twenty-seven patients who had delayed reactions were tested during the acute stage of a disease, and the remainder during convalescence. It is rather difficult to see why erythema should develop at the site of injection as late as two weeks after the tuberculin test has been performed. That it does, at least, suggests that the tuberculin tests should be read at daily intervals for longer than forty-eight hours.

We can do little more than speculate on the reasons for this lack of skin response to tuberculin in certain persons during acute febrile diseases. It is probably significant that the negative tests in patients (who had positive tests during convalescence) occurred in those who not only had fever but were also suffering from diseases which caused considerable general reaction. It is possible that the explanation may be relatively simple and that, as we suggested in our previous paper,

TABLE 3.—*Delayed Tuberculin Reactions*

Day After Injection on Which Test Became Positive	Number
4	10
5	5
6	6
7	3
10	1
11	1
14	1
Total	27

fever and the accompanying disturbances of infection may be the non-specific factors responsible for the failure of skin reaction. Fever alone would scarcely explain destruction of the injected tuberculin since it remains active after autoclaving for fifteen minutes at 15 pounds (6.8 Kg.) pressure. The febrile state and the metabolic changes might, however, affect in some unknown manner the reacting substance (antibody) in the body so that the allergic reaction at the site of the injection of the tuberculin would not occur.

In the discussion of this subject, it is often suggested that injection of tuberculin may sensitize the patient so that subsequent injections will cause a skin response. A consideration of this would involve a rather futile review of theories and arguments concerning sensitization without actual invasion of the body by tubercle bacilli. We may say that our own experience does not lead us to believe that such a factor is of any practical importance in the interpretation of tuberculin tests of the skin and that, whatever the theoretical and experimental evidence may be, one or two injections of small amounts of tuberculin will not in themselves cause previously negative tests to become positive.

CONCLUSIONS

As a result of two years study in which several thousand tuberculin tests were performed, we believe the conclusion warranted that there is often a depression of skin response to tuberculin in acute diseases. During the acute stage of such diseases as measles, diphtheria, scarlet fever and other acute conditions accompanied by febrile reactions, the tuberculin test which had previously been positive may become negative, returning to positive again during convalescence. This is shown by the fact that eleven of sixteen children who were known to have positive tuberculin reactions had no skin response to tuberculin during acute febrile illness. It is further supported by the fact that of 159 children who had positive tuberculin reactions during convalescence from acute diseases, only forty-nine had positive tests during the febrile stage of these diseases. To put this latter statement in another way, of 934 patients, 49, or 5 per cent, had positive tuberculin reactions during the acute febrile stage of various diseases, and 159, or 17 per cent, of these same patients had positive reactions during convalescence. All of the forty-nine patients who had positive reactions during the acute stage also had positive ones during convalescence. The depression of skin response does not seem to be peculiar to any disease or diseases, but depends rather on the severity and the fact that there is a febrile state present.

That this is a depression but not an absence of response seems likely, because a positive skin reaction may be obtained by injecting a larger dose of tuberculin during the acute stage than is necessary to cause a reaction during convalescence, and because a greater degree of skin reaction with the same amount of tuberculin may be obtained during convalescence than during the acute febrile stage of a disease.

The skin response to tuberculin may be delayed for several days.

INTUBATION UNDER CONTROL OF SIGHT*

A. F. PUSHKIN

Oto-Laryngologist of the Rauchfuss Hospital for Children

LENINGRAD, U. S. S. R.

Though stenosis of the lungs is not a definite disease, it is a symptom that is encountered during various diseases, not only of the larynx, but of the whole organism.

Nevertheless, this grievous symptom which renders access to the lungs, the principal physiologic factor of life, so difficult brings about such intense suffering of the whole organism that in diagnosis it has acquired a place almost equal to that of an independent unity.

According to the time of development, stenosis may be divided into acute, subacute and chronic forms.

I shall not stop to discuss chronic and subacute stenoses, as they almost never require intubation; on the contrary, persons with acute stenoses are often cured by this method. Cases of acute stenoses often come under the observation of pediatricians and still oftener—especially in private practice—under that of physicians specializing in infectious diseases, as for instance, during diphtherial croup and somewhat less often during acute infections. Nevertheless, laryngologists are most interested in the fate of these patients. This may be seen from the circumstance that at the All-Russian Conference of Oto-Laryngologists in Odessa during August, 1929, the problem of stenosis of the larynx was included in the program.[1]

The treatment for acute stenoses is a severe task for the physician, whereas in the stage of asphyxia it may without exaggeration be called distressing, as it requires operative intervention. In addition to the initial treatment for the disease from which the stenosis arises, this symptom requires other measures independent of its etiology.

Conservative measures, such as inspiration of vapors, inhalations, administration of narcotics, oxygen and pure air, and revulsive measures, as for instance sinapisms, envelopments, baths, etc., must be tried, if

---

* Submitted for publication, April 30, 1930.

* Read at the meeting of the physicians of the Rauchfuss Hospital for Children on Nov. 29, 1929, and dedicated to the memory of Dr. K. A. Rauchfuss.

* From the Infections Department of the Rauchfuss Hospital for Children. Dr. N. Lunin, Director.

1. Ivanov: Acute Stenosis, J. Dis. Ears, Nose & Larynx, Charkov, 1929, nos. 7 and 8.

time permits. But if the child begins to suffocate, the only fundamental treatment is operative intervention. At present I shall consider two operative methods: the bloody one, tracheotomy, and the bloodless one, intubation. Though not identical, they are equally trying for both the physician and the child, especially for the latter. Some time ago these methods, which are opposed, gave rise to ardent controversies, and each had adherents and opponents. Indeed, except that each has positive and negative properties, they cannot supersede each other. They also differ in their action, though directed to the same end.

Intubation is a method of mechanical dilation of the stenosed larynx in order to supply the lungs with air by natural means. Tracheotomy consists of the formation of an artificial passage for the air at the expense of healthy tissue.

Tracheotomy is an ancient operation, known since the first century of the present era. Galen called Asclepiades creator of the section of the throat. However, until the nineteenth century this operation was not unanimously accepted, and due only to the work and improvements of Bretonneau and Trousseau, especially of the latter, did its application obtain its proper place among pressing surgical operations that every physician must perform. I shall not consider the improvements of the technic, the various operative methods or the modifications of the tracheal tubes; this would lead too far and would exceed the limits of my report. I shall say only that tracheotomy, especially in great urgency, is not easy to perform on children. However, the shortness of the throat, as well as the small length of the correlation of the distance of the tracheolaryngeal tube usually necessitates inferior tracheotomy. When the operation has been performed well, the effect is rapid and sure, and can therefore serve as a last link in a series of attempts to save an asphyxiated child when other methods have failed.

On the contrary, intubation of the larynx is a comparatively new procedure. The history of its development and introduction into Russia is closely related to the name of K. A. Rauchfuss.

Intubation, as well as its variant, catheterization, of the larynx, has arisen from the intubation method of the larynx, proposed for tracheotomy seventy years ago by the surgeon Desault. Bouchut made attempts to introduce this method into medicine, but without success. Trousseau fanatically opposed him, and after violent debates the tubation method was defeated. However, voices arose in favor of Bouchut, and one of the speeches made by the renowned surgeon Maljeune must be noted for its philosophic importance. He said: "The introduction of tracheotomy has been a great merit in the eyes of humanity, but would have been a still greater one if we had learned to do without it."

In 1871, Weinlechner made a modification in intubation of the larynx and proposed it once more, but as a symptomatic measure during asphyxia. Huttenbrener, Rauchfuss and Hack, however, stepped forth as opponents of this method, supporting their opinion by rather weighty arguments. Monti alone admitted that, although intubation of the larynx did not justify the hopes that were founded on it, this method is an important step in the treatment of patients threatened with immediate asphyxia. Maljeune and Monti have proved this to be right. By improvement in this method and by very close observation of patients, Schroetter firmly established the method of catheterization of the larynx. He introduced his ebonite catheters constructed at right angles, which are used even at present, as the most rapid method of dilation in case of sudden asphyxia. Later, metallic laryngeal catheters appeared. The end of the catheter had a triangular structure corresponding to the anatomic structure of the larynx. The catheters were of different sizes according to the patient's age. The catheter used to be introduced in the same way as the intubation tube, but for only a short time, thus affording a possibility of saving time for the necessary preparation before operation. In 1885, the American physician O'Dwyer, who knew nothing of Bouchut and Weinlechner's experiments, proposed new intubation methods which are still in use and which bear his name. He proposed to introduce into the cavity of the stenosed larynx specially constructed metallic tubes of varied sizes and to leave them in the larynx for from twenty-four to forty-eight hours.

This modified intubation method has been accepted by everyone and is widely applied at present in all countries, thus leading to a considerable reduction in the number of tracheotomies. K. A. Rauchfuss took the greatest interest in the establishment of this method in Russia, where he was one of the first intubators. Moreover, he improved the tube by moving its broad part lower down, thus leading to a much fuller dilatation according to the anatomic structure of a child's larynx (fig. 1). Since then, the intubation method has been gradually improved; the closed method has been substituted by the open one, etc.

The majority of improvements concerned only the tubes; these were made for the purpose of (1) avoiding decubiti, (2) keeping the tubes from becoming obstructed by mucus and (3) obtaining their closest correspondence to the anatomy of the cavity of the larynx. One author had his tubes made with a sharp end, like a stirrup (Frohn) (fig. 2); another made them longer than usual (Citelli), and a third (Escott) proposed tubes with lumina.

From the beginning of intubation K. A. Rauchfuss objected to the coarseness of the metallic tubes, and therefore had them made of ebonite. Lately celluloid tubes have been proposed in America.

The metallic tubes used to be silver plated, nickel plated and gilded. It is true that these tubes are lasting and bear sterilization well, but they are undoubtedly too coarse for such a tender organ as a child's larynx. Caoutchouc tubes are softer, but fragile and difficult to sterilize.

A B C

Fig. 1.—*A*, tube (metallic) proposed by O'Dwyer; *B*, tube proposed by O'Dwyer and Baeta, and *C*, tube (ebonite) proposed by Rauchfuss.

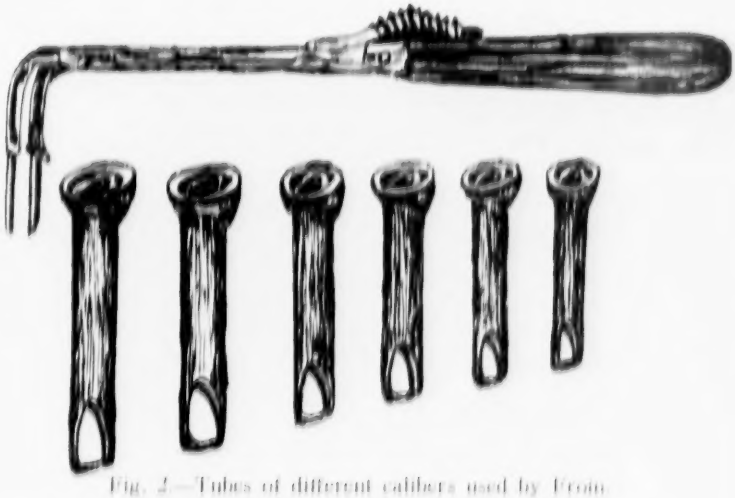


Fig. 2.—Tubes of different calibers used by Frois.

Celluloid tubes are delicate, light and flexible, but do not allow sterilization. Considering the broad development of industry in America and the cheapness of goods, it is possible to have a supply of tubes of all sizes, using for each patient a new tube which is employed only once.

COMPARISON OF OPERATIVE METHODS

Intubation	Tracheotomy
1. The operation is under the guidance of touch (in obscurity); is less precise.	1. The operation is under the guidance of sight; is precise.
2. The operation is not bloody and leaves no scars (method of dilating the larynx).	2. The operation is bloody, leaves scars and impairs the health of tissues.
3. The operation is rapidly performed.	3. The operation needs more time.
4. No deaths occur during operation.	4. Deaths occur during operation.
5. Severe complications seldom occur.	5. Complications occur oftener (hemorrhage, emphysema, etc.).
6. The future of tube-bearers is less gloomy.	6. The future of the cannula-bearers is gloomy.
7. The performance requires great skill and experience.	7. The technic is more simple.
8. Postoperative observation is difficult.	8. Postoperative observation is less difficult.
9. The tube weighs less and is often obstructed by the mucus. The mucus and the tube can be coughed out; therefore repeated intubation may be necessary.	9. The obstruction of the cannula is more rare and its cleansing easier.
10. Decubitus appears more frequently after the tube has been in place for a long time.	10. Decubitus seldom occurs.

From the foregoing comparison, borrowed from Professor Ivanov and partly completed by me, it will be seen that the greatest defects of intubation lie in points 1 and 7 relating to the technic which probably has remained unchanged since O'Dwyer's time.

The performance of an operation in the dark with the help of touch alone obliges one to search for a possible means of replacing touch by sight, the most perfect sense; therefore it is natural that laryngologists perform the operation under the guidance of a laryngeal mirror, i. e., in the same way as indirect examination of the larynx (laryngoscopy) is carried out in adults. In children this is almost impossible for many reasons. In my attempt to eliminate the most disagreeable part of the technic—i. e., the simultaneous introduction into the little patient's mouth of the left forefinger of the surgeon (fig. 3), the tube and the intubator—I found that there is a possibility of partly controlling the eye by applying the simplest instruments and methods accessible not merely to a laryngologist, but to every physician. In order to introduce a tube for a catheter into the laryngeal cavity, it is important to surmount certain obstacles: (1) to draw the epiglottis forward, thus widely

dilating the orifice of the larynx, and (*2*) to seek in the depth some point that might serve as guide for the introduction of the tube into the larynx. The epiglottis may serve as this point. However, there

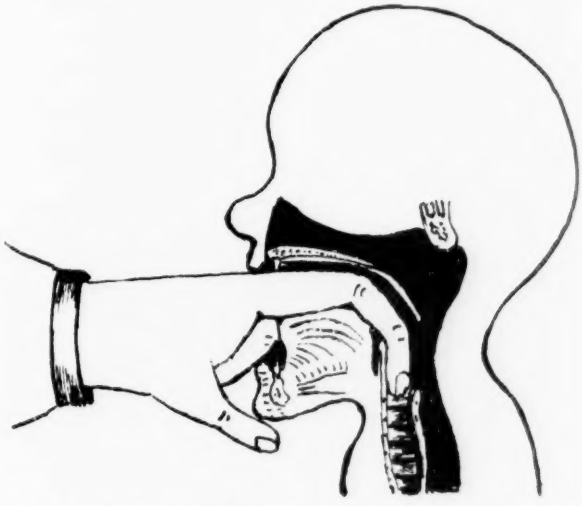


Fig. 3.—One of the old methods of working in the dark, by touch.

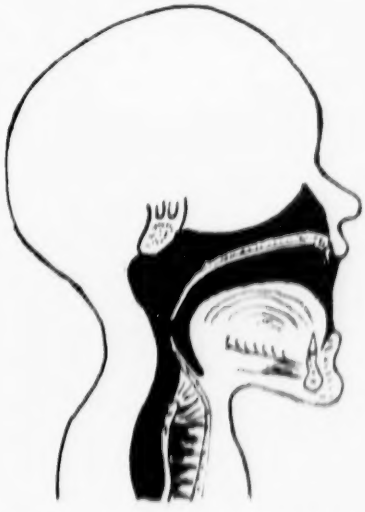
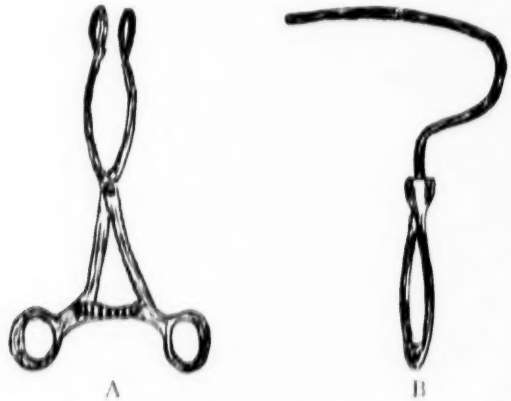


Fig. 4.—Position of the tongue hindering the visible performing of the operation.

is an impediment in the angle of the root of the tongue, which conceals the lingual surface of the epiglottis (fig. 4). To remove these difficulties, I propose the following procedure.

METHOD OF INTUBATION

Supplementary instruments to be used are Collin's tongue-holder and Fraenkel's tongue-holder (fig. 5). The preparations for the operation are the same as usual. As soon as the child has been placed in a position suitable for the operation and the dilator has been introduced, the end of the tongue is seized



A B

Fig. 5.—Instruments that allow one to perform the operation under the control of sight: *A*, Collin's tongue-holder, and *B*, Fraenkel's tongue-holder.

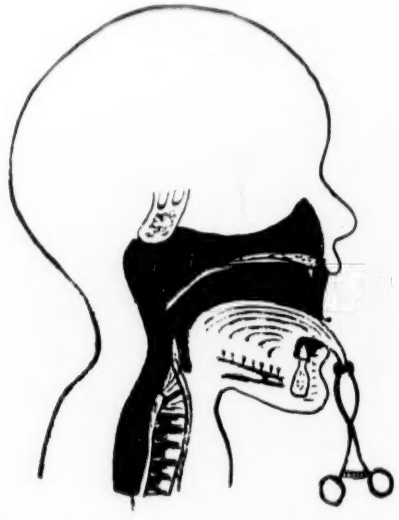


Fig. 6.—Position of Collin's tongue-holder.

with Collin's tongue-holder. I propose the use of this tongue-holder for the reason that it is provided with a long scale of fastenings and a lock, which inevitably permits delicate pressures on the tongue without unnecessary pain. One must not seize the tongue too deeply, however, or one will damage either the frenulum or the sublingual folds of the mucous membrane. When the tongue

holder has been fixed, the tongue must be drawn out with its help as far as possible, after which the tongue-holder is left to hang loosely on the protruded tongue (fig. 6). By this movement the epiglottis is pulled forward and slightly upward, and by the weight of the hanging tongue-holder it is kept in this position. The tongue draws the epiglottis forward by straining the folds of the mucous membrane, especially of the medial one. By this means the tongue becomes slightly flattened. However, this is not enough; it is necessary to see the epiglottis as a topographic point of recognition. Behind it lies the orifice of the larynx. The operator takes Fraenkel's tongue-holder with the left hand and sets it as deeply as possible on the root of the tongue, almost reaching the medial fold, the plica glossa epiglottica mediana. Then by a double movement forward and downward, he squeezes the tongue, thus rectifying the angle of its root and giving it a straight direction (fig. 7).

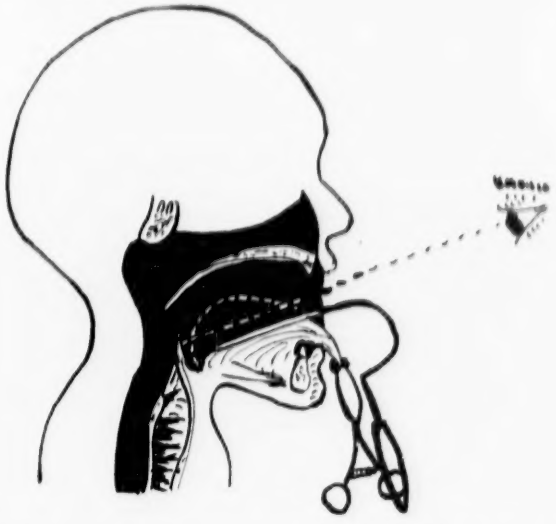


Fig. 7.—Position of both tongue-holders allowing one to see the orifice into the larynx.

Now by looking into the depth of the pharynx at the end of the tongue-holder, one sees the lingual surface of the epiglottis (point of recognition), and by a rapid movement along the medial line can insert behind the epiglottis the tube of the catheter (figs. 8 and 9) and perform the most important intubation movement under an angle of 25 degrees forward and downward according to the anatomic structure of the orifice of the larynx (fig. 10). For that purpose it is necessary to lift up the intubator to the edge of the upper teeth or gums. This done, if the medial line is strictly followed, one must inevitably pass into the larynx.

For the flattening of the tongue one may use the special tongue-holders proposed by Escott and Kirschstein, which are used only by specialists. But the importance of this step lies not in the instrument, but in the procedure, which must be strictly followed. In the closed method of intubation, to remove the mandrin from the tube, as well as to maintain the tube in the laryngeal cavity, the finger of the left hand may be introduced into the pharynx, but this becomes unnecessary with the method of open tubation.

The method of open intubation is a more perfect one. In this case the introduction of a tube may serve as a good indication of its correct position within the larynx (respiratory noise). The mandrin can be easily extracted without hindrance at any moment, if its action is verified beforehand.

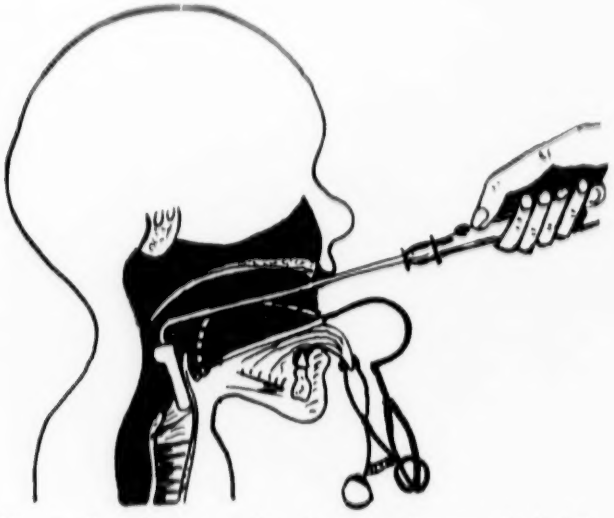


Fig. 8.—Introduction of the tube under the control of sight.

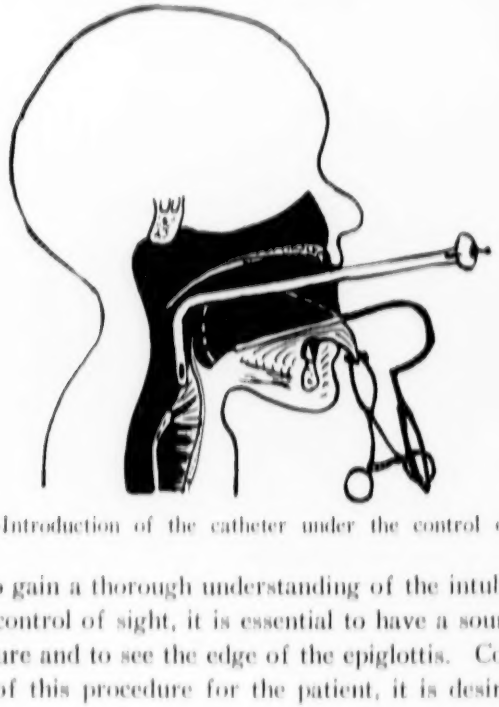


Fig. 9.—Introduction of the catheter under the control of sight.

In order to gain a thorough understanding of the intubation method under partial control of sight, it is essential to have a sound knowledge of this procedure and to see the edge of the epiglottis. Considering the harmlessness of this procedure for the patient, it is desirable to apply

it as often as possible, not only during asphyxia, but in all cases when it is desirable to examine minutely the cavity of the throat and the pharynx, as for instance in angina, retropharyngeal abscesses, etc. If the technic of seeing the depth of the epiglottis is well mastered, one can better learn to introduce into the larynx both the catheter and the tube without being hindered by one's forefinger. Besides, in this method it is much easier to acquire the skill that is so difficult to gain when one is working in the dark (point 7 of the foregoing comparison). There is no doubt that the coryphei of the method of intubation, who are accustomed to perform this operation easily and rapidly, almost "gropingly," call this method simple. I suppose that it is difficult to

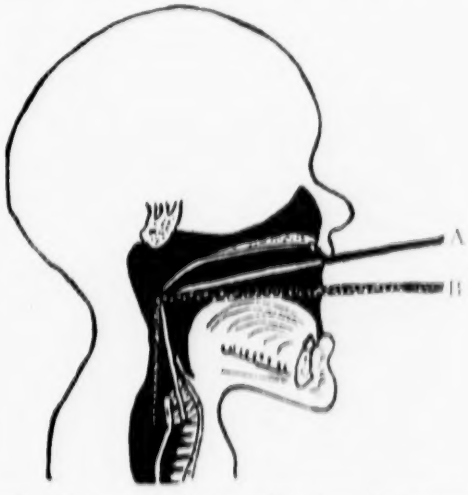


Fig. 10.—*A*, the angle (25 degrees) of the orifice into the larynx along which the tube is introduced forward and downward; *B*, right angle or false downward direction of the tube.

acquiesce with this opinion. When teaching an operator "to grope" one cannot lend him one's finger; moreover fingers are not the same size, and a child's pharynx is neither wide nor extensive.

Having at my disposal no suitable cases for intubation, I could make no attempts to introduce tubes into living children by the method described, but I have introduced catheters easily and rapidly in that way. For this reason I solicit my colleagues who have the necessary material to try this procedure for the intubation of children, the more so, as it is intended to improve the respiratory movement during asphyxia as opposed to the obstructive insertion of the finger. Does this procedure not resemble the method of artificial breathing which consists in seizing the tongue and drawing the epiglottis aside as described by Labord and Bergman?

CONCLUSIONS

1. Intubation under partial control of sight is possible on the basis of anatomo-topographic data.

2. This excludes the painful procedure of introducing the operator's forefinger into the child's mouth, and thus renders the operation hygienic and less injurious to the tissues.

3. The instruments are so simple that the operator is not dependent on a complex apparatus. Whatever he needs may be secured everywhere.

4. This procedure is not only devoid of danger but is even desirable in cases of asphyxia, as the orifice of the larynx is opened more widely, and is not obstructed for even a short time.

5. Intubation may be performed under control of sight slowly and without the least haste. The procedure may be repeated in case of failure.

These suggestions may perhaps prove profitable in the improvement of the technic of this bloodless and salutary operation, in the perfecting of which K. A. Rauchfuss so largely participated, and which he bequeathed to his medical descendants.

THE OPTIMUM CONDITIONS FOR THE PRECIPITATION OF CASEIN FROM HUMAN AND FROM COW'S MILK *

CHI CHE WANG, PH.D.
AND
AGNES A. WOOD, B.S.
CHICAGO

In the study of infant feeding it is often desirable to secure a whey containing as little casein as possible. With cow's milk it is comparatively easy to remove the casein, leaving an edible whey, but this is not true with breast milk. A perusal of the literature reveals that little has been reported on this subject. The few papers that are available direct no attention to the chemical analyses of the whey or the dilution of it. Since their chief attention is directed to either the quality or the quantity of the curd, the whey is usually greatly diluted and not edible. In the present communication a technic is described by which one is able to obtain a clear edible whey with a dilution of only 1 per cent. The minimum dilution reported by previous investigators is 15 per cent.

In their study of the casein of human milk, Bosworth and Giblin [1] precipitated the fat-free milk with 0.6 per cent acetic acid, giving no special attention to the dilution of the whey. Using both undiluted and diluted (1:10) human milk, Demuth [2] obtained a water-clear whey with acid alone and with various buffer mixtures. His minimum dilution was 15 per cent. More extensive work was done by Schemann [3] in her study of the optimum p_H for the precipitation of casein from human milk by means of rennin and acid. The degree of precipitation was estimated only roughly by its appearance, and with an elaborate technic she obtained a clear whey with a minimum dilution of 25 per cent.

In the present study, experiments were conducted on both human and cow's milk, and the degree of precipitation was estimated by the

* Submitted for publication, April 21, 1930.

* From the Nelson Morris Memorial Institute for Medical Research of the Michael Reese Hospital.

* Aided by the Gusta Morris Rothschild Fund and the Otto Baer Fund for Clinical Research of the Michael Reese Hospital.

1. Bosworth, A. W., and Giblin, Louise A.: The Casein of Human Milk, J. Biol. Chem. **35**:115 (July) 1918.

2. Demuth, Fritz: Ueber die Flockung des Frauenmilchcaseins, Biochem. Ztschr. **150**:144, 1924.

3. Schemann, Elizabeth: Untersuchungen zur Verdauungsphysiologie des Säuglings: VII. Zur Magenverdauung, Ztschr. f. Kinderh. **46**:210, 1928.

nitrogen content of the whole milk as compared with that of the whey. The method of Koch and McMeekin [4] was employed for the determination of nitrogen. Aside from using normal hydrochloric acid, acetic and lactic acid of the same normality and lemon juice representing citric acid were employed both alone and in combination with rennin. Titratable acidity and the p_H were also determined. For the former the procedure described by Van Slyke and Baker [5] was followed, while the p_H was determined by the Leeds and Northrope type K potentiometer with quinhydrone electrode.

METHOD FOR HUMAN MILK

Remove the fat of about 120 cc. of milk by centrifugation. Measure accurately, with a graduated cylinder, 100 cc. of the fat-free milk into an Erlenmeyer flask. Make a suspension of 330 mg. (5 grains) of rennin in 10 cc. normal hydrochloric acid. Add from a pipet drop by drop 1 cc. of this suspension into the milk with constant shaking. Transfer the mixture into two 50 cc. centrifuge tubes and incubate them at 38 C. for from fifteen to thirty minutes. Centrifugate the tubes for fifteen minutes and pour the supernatant liquid (whey) into another vessel through a funnel containing a little absorbent cotton. If a strictly clear whey is desired, place the tubes in a refrigerator for at least three hours before centrifugating and filter through a filter paper afterward. By using the same proportion of milk and reagents, any quantity of clear whey may be secured.

COMMENT

In the case of human milk, neither rennin alone nor any of the acids alone gave an appreciable precipitation. Cow's milk was easily precipitated either by rennin alone suspended in water or by any of the acids alone, provided that the optimum quantity of the particular acid was taken. With human milk it was found that regardless of the nature of the acids, precipitation occurred only when a combination of 33 mg. (0.5 grain) of rennin suspended in from 0.5 to 1.5 cc. of normal hydrochloric acid was added to 100 cc. of milk. In every case, 1 cc. of acid gave a better precipitation than either 0.5 or 1.5 cc. The maximum precipitation, which amounted to 50 per cent of the total nitrogen present in the whole milk, followed the addition of 33 mg. of rennin in 1 cc. of hydrochloric acid. With cow's milk, which has a higher buffer value than human milk, the quantity of acids required for precipitation varied with the different acids. The tendency is that the more highly ionizable the acid is, the less is the quantity of acid required for precipitation. Thus, with normal hydrochloric acid, 5.5 cc. per hundred cubic centime-

4. Koch, F. C., and McMeekin, T. L.: A New Direct Nesslerization Micro Kjeldahl Method and a Modification of the Nessler-Folin Reagent for Ammonia, J. Am. Chem. Soc. **46**:2066 (Sept.) 1924.

5. Van Slyke, Lucius L., and Baker, J. C.: Free Lactic Acid in Sour Milk, J. Biol. Chem. **33**:147 (July) 1918.

ters of milk gave a precipitation of 78 per cent of the total nitrogen present in the whole milk, whereas the same amount of acetic acid gave only 53 per cent, and with lemon juice equivalent to 6 cc. of normal citric acid, only 28 per cent. It is, however, singular that lactic acid, unlike the other organic acids, gave the best precipitation of casein. A maximum value of 80 per cent of the total nitrogen present in the whole milk was precipitated by the addition of from 5 to 6.5 cc. of the acid. With rennin alone, 73 per cent of the nitrogen was removed. The great difference between the maximum precipitation of casein by different reagents from the two milks is undoubtedly due to the fact that human milk contains only less than 50 per cent of its protein as casein, whereas the same protein amounts to about 85 per cent in cow's milk.

The precipitation of casein from human milk occurred at a p_H ranging from 6.70 to 3.93, with a maximum value of 50 per cent of the total nitrogen at a p_H of 4.97. The corresponding values for the titratable acidity were 10.84, 2.66 and 5.42 cc. tenth-normal hydrochloric acid per hundred cubic centimeters of milk. In case of cow's milk the p_H varied with the precipitants. When an acid was used, the precipitation occurred at a p_H ranging between 4.97 and 3.97 with an optimum at a p_H of 4.61. The titratable acidity under these conditions was surprisingly high, ranging from 42.76 to 80.20 cc. tenth-normal hydrochloric acid. When rennin was employed, the precipitation occurred at a p_H of 6.53 with a titratable acidity of 7.88 cc. tenth-normal hydrochloric acid per hundred cubic centimeters of milk. Thus, in spite of the much smaller dilution of the whey, the reaction of both cow's and human milk agrees well with that reported by previous investigators. Schemann[5] stated that her complete precipitation of casein from human milk was obtained at a p_H ranging from 5.7 to 5, as compared with our optimum p_H of 4.97. With cow's milk Clark and his associates[6] found that the maximum precipitation of casein with acids occurred at a p_H of 4.6, while ours was 4.61.

SUMMARY

1. Maximum precipitation of casein from human milk may be obtained by adding a suspension of 33 mg. (0.5 grain) of rennin in 1 cc. of normal hydrochloric acid to 100 cc. of fat-free milk at a temperature of 38° C. for from fifteen to thirty minutes. When the foregoing technic is used, an edible whey with a dilution of only 1 per cent may be secured.

6. Clark, W. M.; Zoller, H. F.; Dahlberg, A. O., and Welmar, A. C.: Studies on Technical Casein: II. Grain Curd Casein, J. Indust. & Engin. Chem. **12**:1163 (Dec.) 1920.

2. The maximum precipitation of casein from human milk occurred at a p_H of 4.97 with a titratable acidity of 5.42 cc. tenth-normal hydrochloric acid per hundred cubic centimeters of milk. The amount of casein removed was equivalent to 50 per cent of the total nitrogen present in the whole milk. In the case of cow's milk a p_H of 4.61 gave the best precipitation, 80 per cent of the total nitrogen, when lactic acid was used as the precipitant. When rennin was employed, the maximum precipitation, 73 per cent of total nitrogen, occurred at a p_H of 6.53. The titratable acidity was 48.88 cc. tenth-normal hydrochloric acid per hundred cubic centimeters of milk in the case of acid precipitation and 7.88 cc. in the case of rennin.

A NEW CEREAL MIXTURE CONTAINING VITAMINS AND MINERAL ELEMENTS*

FREDERICK F. TISDALL, M.D.

T. G. H. DRAKE, M.B.

AND

ALAN BROWN, M.B.

WITH THE TECHNICAL ASSISTANCE OF ELIZABETH McNAMARA

TORONTO, CANADA

It has been stated that cereal grains furnish from 30 to 60 per cent of the calories of the average diet.[1] They are the cheapest form of food, and are consumed largely for their energy-producing value. As such they constitute a most important part of the daily diet. It is generally recognized that cereals, particularly the finely milled and refined products, are deficient in many of the minerals and in all of the vitamins. In view of this fact, and with the knowledge that many infants and children receive diets that do not contain enough of the necessary minerals and vitamins to cover the requirements for normal metabolism, we have devised a cereal product which, in addition to supplying energy, furnishes minerals and vitamins in appreciable amounts.

Before considering the composition of cereal products used in breakfast foods or in the diet of infants and children, we must first know from what portion of the grain the cereal is derived. It is relatively unimportant to know what grains are used, because, although wheat is slightly superior to the others, the food value of the different grains is approximately the same.[2] On account of the similarity in structure of the different grains, we shall consider only the component parts of wheat.

The wheat grain consists of three well defined structures, the bran, the endosperm and the germ (fig. 1). The bran constitutes about 13.5 per cent of the grain. It consists of four or five layers, the outer ones of which are mainly cellulose and are not assimilated by the human

* Submitted for publication, July 17, 1930.

* From the research laboratories of the Hospital for Sick Children and the Department of Pediatrics, University of Toronto, under the direction of Alan Brown, M.B.

* Read at the Forty-Second Annual Meeting of the American Pediatric Society, Montreal, June 18, 1930, and the Eighth Annual Meeting of the Canadian Society for the Study of Diseases of Children, Brockville, Ontario, June 20, 1930.

1. The Place of Wheat in the Diet, Editorial, J. A. M. A. **93**:119 (July 13) 1929.

2. McCollum, E. V., and Simmonds, N.: The Newer Knowledge of Nutrition, ed. 4, New York, The Macmillan Company, 1929, p. 109.

digestive organs. The inner layers of the bran are comparatively rich in proteins, phosphates and vitamins. The endosperm makes up about 85 per cent of the grain. It is composed largely of starch cells and contains about 10 per cent protein. The endosperm is poor in mineral elements and is practically devoid of vitamins. It is the portion of the grain utilized in the manufacture of white flour. The germ constitutes about 1.5 per cent of the grain and is the living part which grows and develops into the new wheat plant. It is very rich in proteins, minerals

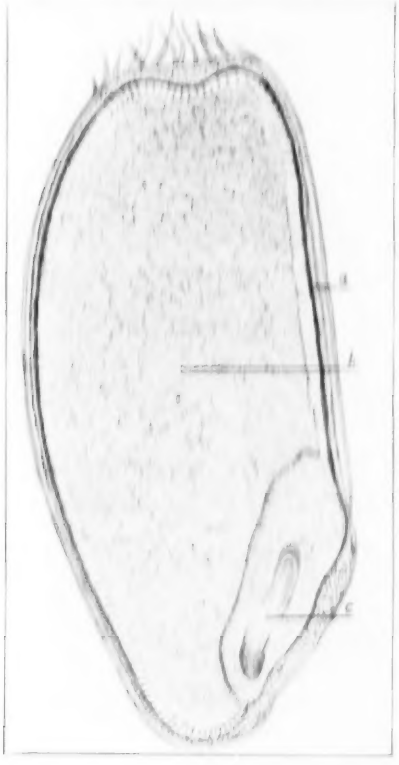


Fig. 1.—Cross-section of wheat grain: *a*, bran layer; *b*, endosperm; *c*, germ.

and vitamins. Owing to the present day demand for white flour products, the endosperm is regarded as the most valuable part of the grain. The bran and germ, with their higher protein, mineral and vitamin content, are carefully separated as being unsuitable for human consumption, and are used for chicken, hog or other feeds.

Cereals as used in the diets of infants and children may be divided roughly into two groups, the whole grain cereals and the part grain cereals. The part grain products are made almost entirely from the endosperm and correspond, as already stated, to white flour. Their

chief advantages are their palatability, keeping quality and nonlaxative effect. Although the protein, mineral and vitamin contents in whole grain cereals are higher than in the refined products, they still fall far below the requirements of the human body. A disadvantage of the whole grain cereals in infant and child feeding is that they sometimes produce a laxative effect that is undesirable. The main objection to the whole grain products, however, is the taste, which is not as acceptable to the average person as the taste of farina or other part grain cereals. The present day infant or breakfast cereals, whether part or whole grain products, are chiefly of value because of their energy producing effect.

The importance of minerals and vitamins in normal metabolism is well recognized. In regard to calcium, the chief source is milk, but between a pint and a quart is required daily to furnish the optimum amount of this element necessary for the growing child. Owing to its bulk, or for other reasons, this amount of milk sometimes cannot be consumed without interfering with the appetite. Unfortunately, all cereals are deficient in this element. Iron is another mineral element that is not so widely distributed in food that its supply can be left to chance.[3] This is particularly true with the small infant whose diet consists largely of milk and cereal, both of which foods are deficient in iron.

In regard to vitamins, although knowledge concerning them is increasing by leaps and bounds, one still knows little of the exact vitamin requirements of the human organism at any age. A marked deficiency of any of the vitamins results in the development of obvious "deficiency diseases," but the recent clinical observations of Hoobler,[4] Morgan and Barry[5] and others indicate that a lowered intake of some of the vitamins may result in the development of irritability, loss of appetite, malnutrition and other states of ill health not commonly attributed to a lack of these dietary substances.

A NEW CEREAL MIXTURE

In view of the previously mentioned facts, we felt that if an infant or breakfast cereal could be devised which, in addition to supplying calories, would furnish minerals and vitamins in appreciable amounts, it should prove to be a valuable addition in the average dietary. However, on account of the general preference for refined and finely milled

3. Sherman, H. C.: Chemistry of Food and Nutrition, ed. 3, New York, The Macmillan Company, 1928, p. 342.

4. Hoobler, B. R.: Symptomatology of Vitamin B Deficiency in Infants, J. A. M. A. **91**:307 (Aug. 4) 1928.

5. Morgan, A. F., and Barry, M. M.: Underweight Children, Am. J. Dis. Child. **39**:935 (May) 1930.

cereals, it was felt that in order to be generally used, the cereal should resemble these widely used products in taste, appearance, nonlaxative effect and keeping qualities. Accordingly, a cereal has been devised that fulfills these requirements and has the following composition: wheat meal (farina), 53 per cent; oat meal, 18 per cent; corn meal, 10 per cent; wheat germ, 15 per cent; bone meal, 2 per cent; dried brewers' yeast, 1 per cent, and alfalfa, 1 per cent.

The wheat meal, oat meal and corn meal form the basis of the cereal. These products are all refined and finely milled, and thus are composed almost entirely of the endosperm of the different grains. The proportions of the different grains used were determined because of the particularly palatable effect secured, which completely masks

Figure 2

Figure 3

Fig. 2.—Xerophthalmia produced by a diet deficient in vitamin A.

Fig. 3.—Cure of xerophthalmia by the addition of the cooked cereal mixture to the diet deficient in vitamin A.

any unusual taste that might be produced by the remaining ingredients. This portion of the mixture in common with other breakfast cereals is low in proteins, deficient in minerals and practically devoid of vitamins.

Wheat germ as obtained from the mills resembles bran slightly, but the flakes are more oily, thicker and of a lighter yellow. As a food for human consumption, wheat germ has been sadly neglected. It contains 10 per cent fat and 30 per cent protein. McCollum and Simmonds[6] stated that "its proteins are abundant and of good quality; its content of the essential mineral elements is much greater than in

6. McCollum and Simmonds (footnote 2, p. 111).

bolted flour; it is exceptionally rich in Vitamins B and E, and it contains some Vitamin A."

It has been generally believed that wheat germ like bran has a laxative effect. This is not so. We have fed several hundred infants, including premature babies under 4 pounds (1.8 Kg.) in weight, 6 teaspoonfuls of raw wheat germ a day for several weeks without obtaining any laxative or other undesirable effect. In fact, in many instances a slight but definite constipating effect was noted. This is probably due to the high protein content. The total mineral content of the wheat germ was found to be ten times greater than that of the mixture of wheat meal, corn meal and oat meal.

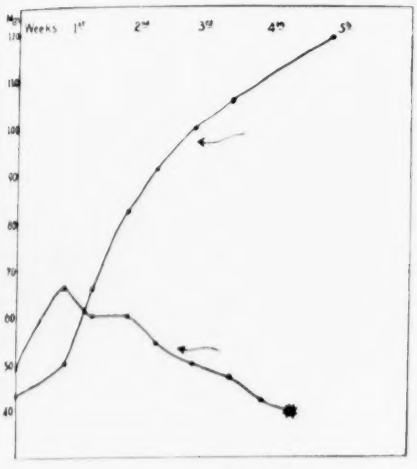


Figure 4

Figure 5

Fig. 4.—Weight chart of rats on a diet deficient in vitamin B and on the same diet with dextrin replaced by the cooked cereal mixture. The lower arrow indicates the curve of the rats fed the diet deficient in vitamin B; the star indicates when death occurred. The upper arrow indicates the curve of the rats that were fed the cooked cereal mixture.

Fig. 5.—Roentgenogram of rat fed on Steenbock's rachitogenic diet.

The bone meal is used on account of its high calcium and iron content. It is obtained by cooking bones in an autoclave at 150 C. for five hours. This removes all the fat. The bones are then ground and dried in an oven at 105 C. for twelve hours. The final product is an odorless and tasteless white powder. We are using this product in preference to pure chemical substances, as there are traces of other mineral elements in the bone meal that may be of importance in the mineral metabolism of the body.

Yeast is used to supply vitamins B1 and B2 in addition to the amount already furnished by the wheat germ. Dried brewers' yeast is

used because it is the most concentrated food source of vitamins B1 and B2. The potency of vitamin B1 is about double that of bakers' yeast. Dried yeast is equivalent to about four times its weight of moist yeast.

Alfalfa is added on account of its high vitamin A and mineral content. We have found that 1 per cent machine dried alfalfa furnished sufficient vitamin A for the cure of xerophthalmia in rats. The iron content of alfalfa is more than 130 mg. per hundred grams, which is ten times the amount found in egg yolk, our most concentrated source of iron in commonly used foods. The calcium and copper content is also high.

It has been found that when all the ingredients used in the product are mixed, ground and thoroughly dried for thirty minutes at a temperature of 70 C. no difficulty is encountered in keeping the mixture for many months. This process reduces the moisture and destroys the insect eggs which are present in all grains.

MINERALS AND VITAMINS IN THE CEREAL MIXTURE

Minerals.—The amounts of calcium, phosphorus, iron and copper found in the cereal mixture and in other cereals are given in table 1.

Vitamins.—The presence of the different vitamins in the final cereal was demonstrated by feeding rats the cereal after it had been cooked in a double boiler for one hour. The presence of vitamin A was demonstrated by placing rats on a diet deficient in vitamin A with added viosterol. After eight weeks the rats lost weight and xerophthalmia developed (fig. 2). Cooked cereal was then used to replace the dextrin in the diet. The xerophthalmia almost immediately improved, and was completely cured in a week (fig. 3). The rats gained 40 Gm. during the succeeding five weeks.

The presence of the vitamin B complex in the cereal was demonstrated by placing rats on McCollum's vitamin B deficient diet,[7] replacing the dextrin ordinarily present with cooked cereal. The rats grew and developed at the normal rate, while the control rats lost weight and died (fig. 4).

Rats fed a diet with the cereal as the only source of vitamin E have developed and reproduced in a normal manner, thus demonstrating the presence of the reproductive vitamin E.

Vitamin D may be secured by the irradiation of the wheat germ or yeast by the ultraviolet mercury quartz lamp. The yeast may also be irradiated by exposure to the sun's rays.[8] The production of this vita-

7. McCollum, E. V., and Simmonds, N.: A Study of the Dietary Essential Water Soluble B, J. Biol. Chem. **33**:55, 1918.

8. Bills, C. E.: Personal communication.

TABLE 1.—*Concentration of Mineral Elements in Different Cereals*

	Total Ash, per Cent	Calcium, per Cent	Phosphorus, per Cent	Iron, per Cent	Copper, per Cent
Farina	0.55	0.025	0.126	Trace	0.0001
Wheat meal, 50 parts Oat meal, 18 parts Corn meal, 10 parts	0.60	0.029	0.184	Trace	0.0002
New cereal mixture	3.20	0.780	0.650	0.024	0.0013

TABLE 2.—*The Antirachitic Effect of Lamp-Irradiated Wheat Germ and Sun-Irradiated Yeast*

Diet of Rats	Inorganic Blood Phosphorus, Mg. per 100 Cc.	Percentage Ash in Bone
Normal diet	6.3	57.0
Rachitic diet (Steenbock 2496)	1.0	44.7
Rachitic diet with 10 % lamp-irradiated wheat germ	5.0	55.4
Rachitic diet (1/30th sun-irradiated yeast	5.1	48.3

Figure 6

Figure 7

Fig. 6.—Roentgenogram of rat fed on Steenbock's rachitogenic diet with 15 per cent of corn replaced by lamp-irradiated wheat germ.

Fig. 7.—Roentgenogram of rat fed on Steenbock's rachitogenic diet plus one thirtieth of 1 per cent of sun-irradiated yeast.

min by these means is shown by the following: Rats were placed on Steenbock's rachitogenic diet,[9] and after four weeks were killed. Marked rickets resulted (fig. 5). Similar rats were placed on the same rachitogenic diet; only 10 per cent lamp irradiated wheat germ was used to replace a corresponding amount of corn in the diet. Prevention of rickets resulted (fig. 6). Similar rats were placed on the control rachitogenic diet; only one thirtieth of 1 per cent sun-irradiated yeast was added. Prevention of rickets resulted (fig. 7). The concentration of the inorganic phosphorus in the blood and the percentage of ash in

[9] Steenbock, H., and Black, A.: Fat Soluble Vitamins, J. Biol. Chem. **64**: 263, 1925.

the bones of these rats are given in table 2. By these means the potency of vitamin D in the cereal may be set at any desired concentration.

CLINICAL USE

This cereal mixture has been used almost exclusively for the past three months in the Hospital for Sick Children, an institution with over 300 beds. In the infant wards, from the standpoint of a laxative or constipating effect, no difference was noted from the results obtained with the refined and finely milled cereals ordinarily used. The palatability of the product was evidenced by its being eaten with the same avidity as the ordinary cereal, not only by the infants, but also by the older children.

Further laboratory and clinical observations are being conducted on this product.

SUMMARY

1. It has been stated that cereal grains furnish from 30 to 60 per cent of the calories of the average diet. They are consumed largely for their energy-producing value, and as such constitute a most important part of the daily diet.

2. Whole grain cereals are deficient in many of the minerals and in all of the vitamins. The finely milled part grain cereals, so widely used, are markedly deficient in most of the minerals and are practically devoid of vitamins.

3. A vitamin intake below the amount required for normal metabolism may produce conditions of ill health other than those commonly recognized as deficiency diseases.

4. Because many infants and children receive diets that do not contain a sufficient amount of some of the necessary minerals and vitamins, an infant or breakfast cereal mixture has been devised which, in addition to supplying energy, furnishes the necessary minerals and five of the six known vitamins in appreciable amounts.

5. The cereal mixture is composed of wheat meal, oat meal, corn meal, bone meal, wheat germ, dried brewers' yeast and alfalfa. It resembles the ordinary finely milled part grain cereals in that it is very palatable and does not produce a laxative or irritating effect on the intestinal tract. After the ingredients are ground, mixed and dried at a temperature of 70 C. for thirty minutes, the mixture will keep indefinitely.

6. The minerals are obtained chiefly from the bone meal, wheat germ and alfalfa. One hundred grams (3½ ounces) of cereal contain as much calcium as 22 ounces of milk. The iron content is almost twice that of egg yolk, our highest source of iron in food. Copper is

present in good concentration, 1.3 mg. per hundred grams of cereal. As the average infant and child consumes from 1 to 2 ounces of dry cereal per day, the calcium in this amount of cereal mixture is equivalent to that contained in from 6 to 12 ounces of milk. The amount of iron in 1 ounce of dry cereal mixture is slightly greater than the amount contained in two egg yolks.

7. Five of the six known vitamins are present in appreciable amounts. Vitamin A is obtained from the wheat germ and the alfalfa, vitamins B1 and B2 from the wheat germ and the brewers' yeast, vitamin D from the irradiation of the wheat germ or the yeast and vitamin E from the wheat germ.

8. The cereal mixture has been used almost exclusively for the past three months in the Hospital for Sick Children, an institution with over 300 beds. It has been found to be just as palatable as any of the finely milled cereals at present so widely used. It should prove to be a valuable addition in the average dietary, because it contains in appreciable amounts so many elements that are known to be essential for normal nutrition.

PHOTOSENSITIVATION *

CLAUSS BURKART STRAUCH, M.D.
MILWAUKEE

Prevention and treatment of rickets with ultraviolet light has become a well established therapeutic factor since Huldschinsky [1] in 1919, first pointed out the curative action of ultraviolet rays from mercury-vapor lamps. A short time later, Hess and Unger [2] demonstrated the same effect brought about by sunshine. Recently Tisdall and Brown [3] stated that even skyshine, sun rays filtered and reflected by clouds, has still a marked antirachitic action. The same authors, however, proved by experiments the fact, well known through experience, that during the winter months the power of sunlight is relatively very small. As a substitute for the invigorating power of bright summer sun, mercury lamps are now used more and more during the darker months.

Photosensitivation can be regarded as another method of bringing about the visible effects of sunlight on the skin, but this method and its capacity are as yet very little known. Compared with procedures in photography, photosensitivation, which means sensitivation toward light, renders the organism more sensitive to light. A few series of experiments on photosensitivation will be reported here. My experiments have been begun with the intention of treating patients with rickets by sunlight during the winter months. The technic of effective photosensitivation, the influence of the different wave lengths, the mechanism of the action and the relation of the sunburn obtained to the clinical effect and many other questions are still unanswered. This paper therefore will be limited to describing an effective method that will render persons highly sensitive to light.

In ferments and in animals, it is possible to increase the effect of light by chemical means. Tappeiner,[4] experimenting on the action of dyes on paramecia, was at first puzzled by the different toxicity of equal solutions. He found the explanation in the influence of the quantity of light present. Numerous investigators confirmed and enlarged his experiments. In hogs, for instance, disturbances after feeding with barley stained by eosin, could be ascribed to photosensitivation.

* Submitted for publication, April 24, 1930.

1. Huldschinsky, K.: Deutsche med. Wchnschr. **45**:712, 1919.

2. Hess, A. F., and Unger, L. T.: Cure of Infantile Rickets by Sunlight, J. A. M. A. **77**:39 (July 2) 1921.

3. Tisdall, F. F., and Brown, A.: Seasonal Variation of Antirachitic Effect of Sunshine, Am. J. Dis. Child. **34**:721 (Nov.) 1927; ibid. **36**:734 (Oct.) 1928.

4. Tappeiner, V.: Ergebn. d. Physiol. **8**: 698, 1909; ibid.; in Abderhalden: Handbuch der biologischen Arbeits-Methoden, ed. 5, Berlin, Urban & Schwarzenberg, 1923, vol. 7, chapt. 4. Both papers give complete bibliography until 1923.

increased sensitivity against light was finally found to be an important factor in the symptoms of porphyrinuria, pellagra and other human diseases.

It has been tried, of course, to utilize this possibility in medicine. Especially eosin, which is of value for sensitivation in photography, was used in weak infants to increase the reaction to light, either given by mouth or used as an ointment applied to the skin during treatment with sunlight. French authors report sensitivation toward ultraviolet rays by means of intravenous injections of acriflavine hydrochloride (trypaflavine). An extreme degree of light sensitiveness has been produced by Meyer-Betz [5] on himself after an intravenous injection of 0.2 Gm. of hematoporphyrin dissolved in 10 cc. of tenth-normal sodium hydroxide with the addition of a 300 cc. of physiologic solution of sodium chloride. Exposure to moderately bright sunlight for ten minutes brought about an erythematous edematous reaction, such as is ordinarily seen only after hours of exposure to the sun on glaciers. The lasting effect of the one injection was apparent for months by increased formation of pigment after each exposure to the sun.

The substances named are joined by the quality of fluorescence. Fluorescence seems to be connected with the ability of photosensitivation. Other fluorescing substances used in animal experiments for sensitivation are: methylene blue (methylthionine chloride), rose bengal, chlorophylzeochin (from corn), erythrosin, etc. The nontoxicity of any substance to be used for medical purposes is, of course, of the first importance.

In my own experiments, white rabbits, fully shaved, have been given intravenous injections with watery solutions of eosin (0.2 to 0.5 Gm. eosin per kilogram of weight). The striking pink color obtained, lasting from one to two days, did not render the rabbits markedly sensitive to the light. After exposure to sunlight for six hours, the ears of the pink rabbits were only slightly more edematous than the ears of the controls. In white mice, eosin proved very inferior to hematoporphyrin. White mice given injections with 0.5 mg. of this blood derivative and exposed to sunlight for thirty minutes were regularly so affected by the sun that they were found dead about twelve hours after exposure, while the mice with the same amount of hematoporphyrin, but kept in the dark, and those controls which were exposed without being given injections, were not impaired. Daily injections of 20 cc. of 2 per cent acriflavine hydrochloride given for four days to two children aged 12 and 14 years, respectively, did not render them sensitive to the sun or to the ultraviolet rays. Chlorophyl dissolved in olive oil and injected intramuscularly into two persons was without influence. The effect produced by injections of hematoporphyrin that was made from hemin

5. Meyer-Betz: Deutsches Arch. f. klin. Med. **4**:477, 1923.

according to the method of Willstaetter and M. Fischer,[6] was very distinct, however.

Two sons of a farmer, C. R. and W. R., aged 5 and 3, respectively, had been operated on for correction of high grade rachitic curvatures of the legs. Both showed the same habitus, the same weak constitution and the same muddy color of the skin, which rendered the use of the elder boy as a control test for the experiment rather reliable. On September 1, at 9:30 a. m., the younger one, who weighed 40 pounds (18.1 Kg.), was given intramuscular injections in four different places with a total of 0.12 Gm. hematoporphyrin dissolved in 80 cc. of a weak

Erythema solare after sensitivation with hematoporphyrin. The face, shoulders and a round spot on the abdomen were covered during radiation.

solution of sodium hydroxide. On a round spot on the abdomen of both, a piece of black paper was pasted to make the reaction of the surrounding skin more distinct. At noon, both brothers were exposed to a medium bright sun for twelve minutes. Four hours later, the exposed skin of the boy given hematoporphyrin was markedly reddened and made a striking contrast to the covered spot, which showed no change at all. The brother who acted as a control did not show the slightest reaction. Both children felt well. One week later, the infection of the same

6. Willstaetter, R., and Fischer, M.: Hoppe-Seylers' Ztschr. f. physiol. Chem. **87**:423, 1923.

amount of hematoporphyrin (0.12 Gm.) was repeated in the same boy. This time exposure to sun's rays of a medium intensity for ten minutes produced a rather dangerous erythema solare with extensive edema, several blisters of the size of an egg, numerous small ones and small superficial sloughs. The temperature at 6 p. m. was elevated to 103.5 F. The boy had a headache and had no appetite. The urine contained traces of albumin on the next day. The elder brother, again used as a control, did not show the slightest reaction.

This striking success, as far as successful sensitization was concerned, was similar in two more patients. Every precaution, however, was taken to prevent an equally extreme reaction as in the first case. No damage of any kind was seen further, the exposure to light being made cautiously and gradually. The injection in all these cases was given with the therapeutic intention of stimulating the reaction of the skin to light in children with slowly reacting skin. The relatively small toxicity of hematoporphyrin and the fact that it may be considered as a rather physiologic substance, being excreted in small amounts in every normal urine, gave further support to the therapeutic intention. These few experiments, however, are quoted merely to show that it is possible, in an effective but harmless manner, to sensibilize an organism to light with hematoporphyrin and to instigate further tests on the neglected subject of photosensitivation. The damage done in the second experiment on W. R. is not to be explained by the drug, but by the extensive effect of the sunlight. The sensibilizating substance is apparently only a catalyst for oxidation under the action of the light. It is true that the radiation with ultraviolet rays, etc., effects any desired degree of skin reaction. The extensive use of this method, however, is somewhat limited by expense and the equipment necessary. In addition to this, it has not the exalting and elevating influence on the body and spirit that a certain amount of bright sun has for a man living in a climate with poor sunlight, which may be somewhat connected with the amount of sensibilizating substance derived from the blood and circulating within the organism.

As yet, the experiments do not prove that this method can be applied without disadvantageous side effects. In regard to rickets, it has to be demonstrated that a reaction of the skin shown by reddening and pigmentation due to photosensitivation will be curative like the reaction on ultraviolet rays. But a method that stimulates the organism to increased reaction to one of the most important agents, light, is well worth further investigation.

SUMMARY

Photosensitivation permits increase of the reaction of the skin to sunlight.

Hematoporphyrin is superior in this respect to other substances.

Severe sunburn may result in persons made sensitive.

Photosensibilization may compete with ultraviolet irradiation in the prevention and cure of rickets.

371 Twenty-Sixth Street.

Case Reports

BONE SUPPURATION AND RENAL CALCULI IN CHILDREN *

MILTON C. BORMAN, M.D.
MILWAUKEE

The increasing attention of the medical and surgical profession to pathologic conditions of the urinary tract in children and the possibility of more than incidental association of bone suppuration and renal calculi suggested the advisability of making this report.

UROLITHIASIS IN CHILDREN

Young [1] stated that urolithiasis is very common in children in some countries, but that it is far less common in children in America. Holt [2] noted that at necropsy small stones were found in the urinary tract of children in the first two years of life. Rafin [3] reported 322 cases in infants. Bókay [4] collected 1,836 cases of calculi in infants and children. Twenty-five per cent of Thomson's [5] 3,492 cases of urinary lithiasis in China occurred in children under 10 years of age, the youngest being 2 years old. Thomas and Tanner [6] collected 197 cases of calculi reported in children in this country. They reported six additional cases of their own, and expressed their belief that the condition is common. Johansson [7] reported the finding of a right renal calculus and a left ureteral calculus in a child aged 5. Brown [8] reported the finding of a pure xanthine stone in acid urine of a probably rachitic boy, aged 3, without evidence of preceding infection of the urinary tract. This suggested that the causative factor was a metabolic disturbance. Deherripon [9] described

* Submitted for publication, March 12, 1930.

* From the Montgomery Clinic, Montgomery, W. Va.

1. Young, Hugh H.: Practice of Urology, Philadelphia, W. B. Saunders Company, 1926, vol. 2, p. 661.

2. Holt, L. E.: The Diseases of Infancy and Childhood, ed. 5, New York, D. Appleton & Company, 1909.

3. Rafin: Ann. d. mal. d. org. génito-urin. **32**:46, 1921.

4. Bókay, J.: Ueber die infantile Lithiasis in Ungarn, Ztschr. f. Kinderh. **4**: 365, 1912.

5. Thomson, Joseph Oscar: Urinary Calculus at the Canton Hospital, Canton, China, Surg. Gynec. Obst. **32**:44, 1928.

6. Thomas, Gilbert J., and Tanner, Chester O.: Urinary Lithiasis in Children, J. Urol. **8**:171, 1922.

7. Johansson, L.: Renal and Vesical Calculus in Children, Hygiea **83**:833, 1921; abstr. J. A. M. A. **78**: 1014 (April 1) 1922.

8. Brown, Damon A.: Renal and Ureteral Calculi in Childhood, J. Urol. **18**: 285 (Sept.) 1927.

9. Deherripon: Lithiase rénale (coliques néphritiques, anurie de sept jours) chez un nourrisson de trois mois, Bull. Soc. de pédiat. de Paris **25**:460, 1927.

a case of renal calculi in a nursing child, aged 3 months, in whom the symptoms of hematuria and anuria called the mother's attention to the condition. A single uric acid calculus with only traces of calcium weighing 0.07 Gm. was expelled. Ten days later, twelve other calculi were expelled which weighed from 0.03 to 0.09 Gm. each. The rarity of hematuria and anuria in a child of this age was pointed out.

Ulmer[10] reported a case in which a boy unwell from the age of 1 year was first seen ten months later, when he had a palpable tumor in the hypogastrium. This was verified roentgenologically by a shadow the size of a hen's small egg. It was removed by suprapubic cystostomy after about four months. The child had been pale and in poor nutrition, with albumin, leukocytes, a few erythrocytes and diplococci in the urine. After two months, nephrectomy of the left kidney was performed, and six stones were found. Histologic examination showed a chronic focal nephritis. The child recovered. The author stated that the calculi were so large that the disease must have begun at a very early age.

Bugbee and Wallstein,[11] in a review of 4,983 necropsies on infants and children, found reports of renal calculi in 13 infants, all with one exception under 1 year of age, and one in a child aged 11 days. This suggested to them that calculi may form in the fetus, and that faulty metabolism and maternal infection may be the underlying cause. All these children harbored an infection, and all but three had severe gastroenteritis. The authors believed it fair to assume that renal calculi are more common in infants than is generally supposed, and that many indefinite cases of colic may possibly be thus explained.

UROLITHIASIS ASSOCIATED WITH BONE SUPPURATION OR TRAUMA

Mayet[12] reported roentgenographic evidence of bilateral renal calculi in a boy, aged 11, four years after immobilization for Pott's disease. An abscess in the left iliac fossa was aspirated, and the boy was given an injection. Mayet stated that Mousseaux deVittel was the first to call attention to renal colic in children who underwent prolonged immobilization. He recorded a second case in a girl, aged 14, with a tuberculous hip and an abscess which he also aspirated. She had been immobilized for two and one-half years when she had an attack of renal colic and passed a small stone, verified by the family physician. During a second attack of renal colic six months later, no calculi were found. He cited the observations of Prof. Arnozan de Bordeaux on a patient with

10. Ulmer, O.: Occurrence of Urinary and Renal Calculi in a Very Young Child (Case Report), Arch. f. Kinderh. **85**:87 (Sept.) 1928.

11. Bugbee, Henry G., and Wallstein, Martha: Surgical Pathology of the Urinary Tract in Infants, J. A. M. A. **83**:1887 (Dec. 13) 1924.

12. Mayet, M. H.: Calculus in Both Kidneys in a Child Immobilized for Pott's Disease, Paris chir. **12**:132, 1920.

coxalgia in whom the excessive ingestion of calcium phosphate and immobilization led to the formation of multiple calcium phosphate renal calculi. Mayet believed that it was possible that immobilization with diminished activity, overeating and phosphate therapy led to the production of renal calculi. In the discussion, the following cases were described: LeFur discussed a case in a veteran, aged 20, who had urinary retention following a bullet wound in the bone-marrow. A cystostomy was performed, and, although there was no urinary infection, the patient had bilateral renal calculi. Subsequently, two laminectomies were performed, and at intervals since then the patient had passed large uric acid calculi. Iselin reported his observations on a patient, aged 30, in whom, following twenty-two months' immobilization for a tuberculous knee, a uric acid calculus in the right kidney was removed by pyelotomy. Bonneau discussed a case in a youth, aged 14, who fractured the bones of both legs. After ten months he became obese and dyspneic, and voided urinary gravel and calculi. There had been no preceding urinary abnormality or tuberculous infection. All these disappeared when he again became active. Luys observed a wounded veteran, immobilized for an extremely long time because of a grave lesion of the spinal marrow, who spontaneously voided several phosphatic vesical calculi.

Simon [13] rendered a medicolegal opinion that renal calculi may develop as a result of injury to the spinal cord and fractured vertebrae. A man, aged 34, had renal colic five months after injury. Nephrectomy two months later revealed a previous severe injury to the upper pole of the right kidney, with foci of hemorrhage, focal nephritis and five calculi consisting of organic substance and calcium salts. He stated that there are four possible causes for renal calculi: injury to the kidney, ascending cystopyelitis after injury and infection of the urinary tract, fracture of the spinal column and paralysis of the cord with its renal effects. The nature of the stones depends on the composition of the urine secreted by the injured kidney.

Cabot [14] reported that a man, aged 34, who had had a severe crushing injury of the left hip one year before, voided a vesical stone, and that three years later, at operation, a left ureteral stone was removed.

Noland and Conwell [15] recently reported the apparent tendency toward the formation of renal and bladder stones during the convalescent period in several cases of severely fractured pelves.

13. Simon, E.: Formation of Calculi in the Kidney after Fracture of the Vertebrae and Injury of the Spinal Cord, Ztschr. f. Urol. **21**:444, 1927.

14. Cabot, Hugh: Remarks on the Technique of Operations for Stone in the Ureter, J. Am. Urol. A. **4**:204, 1910.

15. Noland, Lloyd; and Conwell, H. Earle: Acute Fractures of the Pelves, J. A. M. A. **94**:174 (Jan. 18) 1930.

Paul[16] reported twenty cases of nephrolithiasis in men whose ages ranged from 22 to 37. In every case, with one possible exception, Paul stated that there was undoubtedly a definite etiologic relationship between the bone suppuration and the formation of renal calculi. These patients came under his observation during the three preceding years at the hospitals of the Department of Soldiers' Civil Reestablishment in Toronto. In discussing this paper, Leon Herman described a case of stone following *Staphylococcus aureus* osteomyelitis of the right tibia in a boy, aged 8.

The interest in the following case depends on the facts that the renal calculi were bilateral; that there were calculi in both ureters, but none in the bladder; that the patient was a boy, aged 9, with an overwhelming osteomyelitis of the tibiae from which he ultimately died; that the only clinical symptom of urolithiasis was hematuria, the calculi remaining unsuspected and undiscovered until necropsy, and that the calculi chemically were composed of practically pure calcium phosphate with a small amount of organic matter. According to Thomson,[5] less than 5 per cent of urinary calculi are composed of calcium phosphate. In the series of 203 cases reported by Thomas and Tanner,[6] only one showed calculi in both kidneys and ureters.

REPORT OF CASE

A white school boy, aged 9, who had never had good health, complained of malaise, diarrhea, weakness and fever five weeks before admission to the hospital. Two weeks before admission, the weakness became marked. He became emaciated and pallid. He then had a severe attack of epistaxis of eight hours' duration. It was noted that although the first portion of urine during micturition was normal in appearance, the later portion was pure blood. Swelling and tenderness were then noted in the left leg and ankle, followed by a similar change in the right ankle. He was obliged to lie on his right side thereafter because of the pain in the lower left extremity. He complained of slight cough and headache. He had had measles, mumps and influenza. Three other children in the family were living and well. One had been treated by me two years previously for acute nephritis. The patient's mother had died in this hospital six years before from a puerperal infection. There was no family history of, or known exposure to, tuberculosis.

On physical examination, the patient appeared acutely ill, pale, weak and septic, and he perspired freely. He wished to remain on his right side, both lower extremities flexed at the hips, knees and ankles. His sublingual temperature was 99.6 F., his cardiac rate 140 and his respiratory rate 26. There was pitting on pressure of the soft tissues of both extremities below the knees. Passive motion of the hip, knee and ankle joints was painful, especially in the right extremity. The lateral surface of the right leg was spotted with purple macules from 1 to 3 mm. in size. There was edema of the scrotum. Multiple small ulcers of the skin were noted over the bony prominences of the sacrum, hips and right lower

16. Paul, H. Ernest: Bone Suppuration the Basic Cause of Renal Calculus in Twenty Cases Following War Wounds, J. Urol. **9**:345, 1923.

extremity. A roentgenogram revealed osteomyelitis of the left femur. Urinalysis yielded negative results except for a slight cloud of albumin, an occasional erythrocyte and a few pus cells with calcium phosphate and triple phosphate crystals. His blood count was as follows: red blood cells, 2,500,000; hemoglobin, 50 per cent (Sahli); white blood cells, 24,800; polymorphonuclear leukocytes, 89 per cent; lymphocytes, 9 per cent, and monocytes, 2 per cent.

Eleven hours after admission, he was given a transfusion of 500 cc. of unmodified blood by the direct method. After receiving another transfusion of 500 cc. of unmodified blood by the direct method, under nitrous oxide-oxygen anesthesia, iodine technic, the lateral part of the left thigh was incised. When the muscles were split, thick creamy pyoid material escaped under pressure. A sequestrum

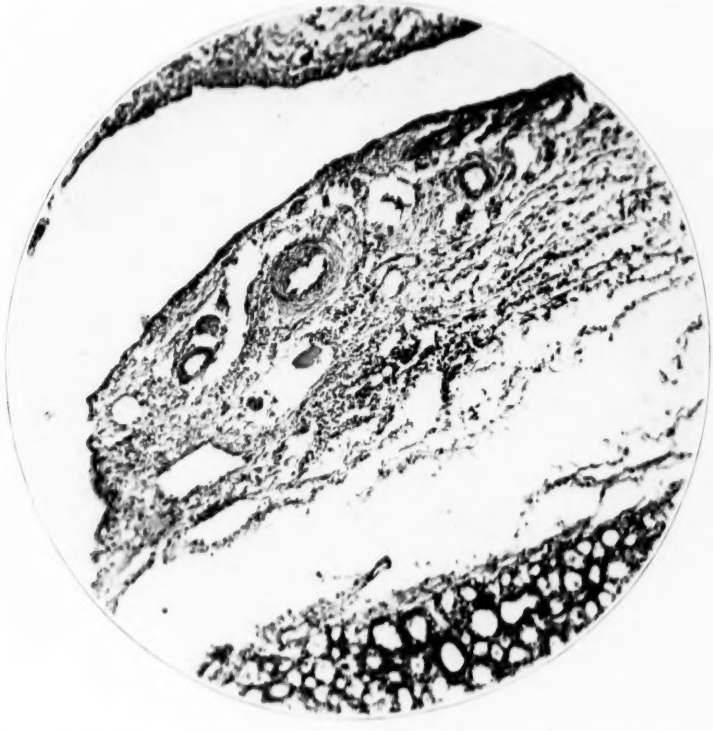


Fig. 1.—Peripelvic renal tissue with a collection of small round cells in the center of the field. This kidney pelvis was filled with calcium phosphate calculi.

was removed, the medullary cavity exposed and curetted, the wound swabbed with tincture of iodine, followed by 65 per cent alcohol, and packed with petrolatum gauze, a dressing placed over the wound and a double spica body cast applied. The postoperative treatment was that advocated by Orr.[17]

Although the patient lived for ninety days following the operation, he gradually grew weaker and remained more or less septic. Repeated blood counts revealed a

17. Orr, H. W.: Treatment of Osteomyelitis by Drainage and Rest, W. Virginia M. J. **24**:313 (July) 1928.

persisting increasing anemia, varying from 50 to 80 per cent hemoglobin and from 2,500,000 to 3,800,000 erythrocytes, combated by three postoperative direct blood transfusions of 260, 500 and 500 cc., respectively. On the fourteenth day, because of the odor and a soiled cast, the wounds were dressed and a new cast was applied. Although the patient's appetite remained good, he became more emaciated. On the forty-first day, the second cast was removed. There was marked edema of the left groin and buttock. Ulcers were noted over the dorsal pelvic spines and the lumber spinous processes. The wound in the left thigh was draining pyoid material. He was placed in a bivalved cast. Two days before death, clonic contractures in all extremities were noted and tachycardia and cyanosis appeared. Death occurred ninety days after operation.

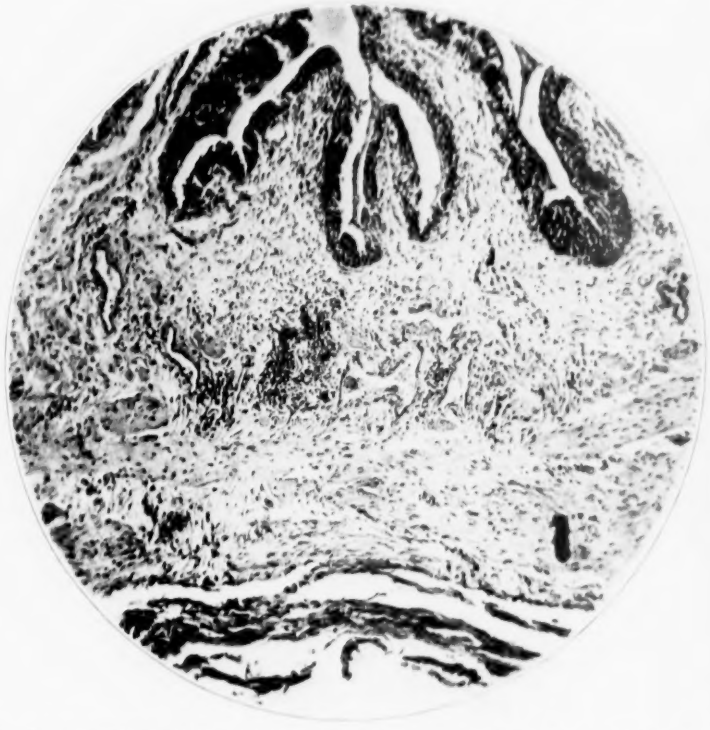


Fig. 2.—A portion of the ureter attached to the kidney from which figure 1 was obtained. The ureter also contained several calcium phosphate calculi. Near the center of the field a collection of small round cells may be seen.

Report of Necropsy.—The examination was begun two and one-quarter hours after the patient died. The body externally showed marked cachexia, with no evidence of subcutaneous fat. There were alopecia and an ulcer over the occiput. There was ulceration of the skin exposing the periosteum, bone and ligaments from the middorsal spine down to and including the sacrum. There was an ulcer over the dorsum of each heel. There was a sinus over the anterior surface of the right hip, and when the joint was manipulated there was a grating sound and a white pyoid material gushed forth. There was an old incision over the lateral anterior

Fig. 3.—Renal and ureteral calculi as shown by a roentgenogram after the urinary tract had been removed at necropsy in toto except for the right kidney. The right kidney was removed and sectioned at the time of necropsy.

surface of the upper part of the left thigh from which a grayish-white watery fluid exuded. The right femur was opened. The marrow appeared normal. There was bony sequestration with pyoid material, however, in the right hip joint. There was no evidence of infection from the peritoneal aspect of the pelvic structures. The remaining bony framework was normal, except for crepitation in both knee joints attributed to the atrophy of disuse.

The pericardial sac, pleurae and peritoneum were normal. The heart muscle was somewhat flabby and yellowish, and when examined histologically had a boiled appearance. Scattered throughout the lungs were firm, granular, non-air-containing, dark red patches, which when examined histologically were seen to contain acute inflammatory exudates. The esophagus, stomach, small and large intestines and pancreas were normal. The spleen was moderately congested. The follicles were moderate in size. The liver was nutmeg-like in appearance and showed marked deposition of pigment intracellularly, with cellular atrophy and fatty change periportally. The left kidney capsule stripped with ease leaving a smooth underlying surface, paler than normal. The cut surface was pale, the markings being indistinct in patches. The pyramids and their papillae were yellowish-gray. The pelvis of the kidney was filled with yellowish-green calculi,

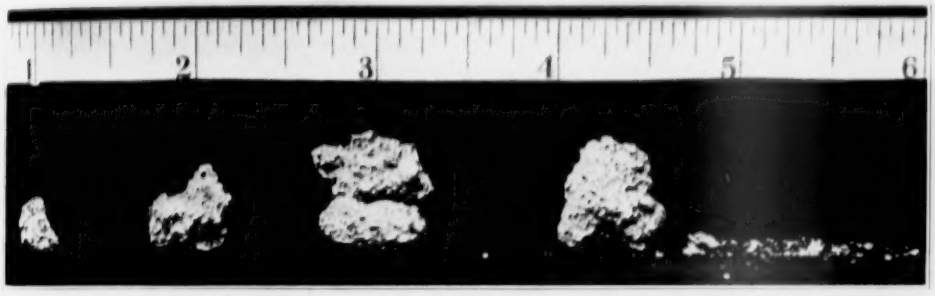


Fig. 4.—Several calcium phosphate calculi from the right ureter and kidney pelvis after having been dried for four days in an incubator.

varying from 1 to 14 mm. in size. The right kidney resembled its fellow and its pelvis was also filled with similar calculi as were both ureters which presented an irregular contour of varying diameter. The bladder mucosa was pale, smooth and glistening, and there were no vesical calculi. In the connective tissue beneath the pelvic mucosa about a papillary tip of the kidney histologic examination revealed a small amount of perivascular round cell infiltration (fig. 1). An occasional hyaline cast was noted in the collecting tubules. The secreting tubular epithelium was swollen and cloudy, and there was some desquamation. There was a normal amount of interstitial substance. A single hyalinized glomerulus was noted. The remaining glomeruli were normal. The vessels appeared normal. The capsule was slightly thickened in a few areas. The right ureter showed a moderate sprinkling of small round cells in the submucosa and throughout the muscular and subserosal layers. A single definite small round cell collection was noted (fig. 2). The lumen was stellate, owing to the invaginating mucosa. The transitional lining of the bladder appeared normal. There was a small amount of diffuse round cell infiltration. The only histologic abnormality in the urinary tract was the mild small round cell infiltration suggesting a mild response to a mild stimulus. A roentgenogram of the urinary tract was made (fig. 3). The

calculi in the right kidney weighed 6.026 Gm.; those in the right ureter weighed 2.040 Gm. The calculi were placed in an incubator and dried for four days. Several calculi were photographed (fig. 4). They were then sent to Dr. J. A. C. Colston of the James Buchanan Brady Urological Institute, Department of Urology, Johns Hopkins University Hospital, Baltimore. On chemical examination, he reported that "they consisted of practically pure calcium phosphate with a small amount of organic material." One of the larger stones was then crushed, placed on a slide with water, covered with a cover-slip and examined under low and high power magnification. The material was composed of many clumped areas of round refractile bodies which were larger than erythrocytes, and made up of concentrically arranged rings. Only a single tuft of the needle formation of crystalline calcium phosphate was seen. There was some amorphous material, bacterial growth and mucin-like shreds. When a drop of concentrated nitric acid was added, the material cleared up. No crystals or round bodies were then seen.

COMMENT

It is interesting to note that the only clinical evidence of urolithiasis in the case reported was the hematuria which occurred about four weeks after the onset of the illness. If urolithiasis was dependent on bony suppuration, it apparently developed rapidly. The phosphaturia and the destruction of calcified bone with its probable absorption seem significantly associated with the calcium phosphate urolithiasis. It seems unusual that such extensive calculus formation would exist without the production of renal colic. It is possible, however, that such colic did occur in the later stages of the patient's illness when he was under the influence of sedatives and too ill to make complaint. The small amount of pyelonephritis as revealed by histologic examination seems insufficient to account for the production of the calculi. The pyelonephritis would seem rather to be a result of the irritant action of the calculi.

SUMMARY

Brief mention is made of the growing interest in pathologic conditions in the urinary tract in children. References are made to the incidence of renal calculi in infancy and childhood, and to their frequency in patients with fractured spine and with bone suppuration. A case is reported of bilateral renal and ureteral calcium phosphate calculi in a boy, aged 9, who had extensive osteomyelitis. The only clinical symptom suggesting calculi was hematuria, but the condition remained undiscovered until necropsy. The calculus formation in this case was probably definitely dependent on the osteomyelitis, and was not simply an associated incidental condition. This case and others reported in the literature would suggest the importance of always suspecting the association of urolithiasis with bone suppuration in both children and adults. Such patients should be given plenty of fluids. If calculi form, the reaction of the urine should be changed.

HYPERPLASIA OF THE CORPORA ADIPOSA BUCCARUM

IN A NEW-BORN INFANT*

FRANK C. NEFF, M.D.
AND
JOHN A. BILLINGSLEY, M.D.
KANSAS CITY, MO.

The sucking pads in an infant a few days after birth were found to be coincidentally enlarged, both visibly and palpably, but not sensitive to touch. By their prominence at this early time of life, they offered a clinical picture which was striking. There was no wasting of the surrounding superficial fat which would cause the fat pads to stand out in contrast, such as is noticeable in atrophic infants.

REPORT OF CASE

History.—A Negro boy, born in the University of Kansas Hospital on April 7, 1929, weighed 5 pounds (2,268 Gm.) at birth. The mother was then in a pre-eclamptic condition. There was no syphilis in the family. This child was the twelfth pregnancy; the first ten children were living. The delivery was simple, lasting one hour and forty-three minutes. No instruments were used, and the infant was not injured. However, he had a poor color at birth, was flabby and had to be given artificial respiration because he did not attempt to cry or move his limbs. He did not nurse for three days, sleeping most of the time, probably due to immaturity or to toxic influences retained from the uremic mother's blood. The temperature was never above normal, and usually subnormal, from 95 to 97 F. (35 to 36.1 C.) until the third day when it reached 99 F. (37.2 C.), after which it was always normal. There was no stomatitis or glandular enlargement.

By the sixth day of life, a firm tumor of irregular outline had developed in the center of each cheek. These enlargements could easily be seen as well as felt. When first observed, the two masses were about 4 cm. in the greatest diameter, but in a few days they had attained twice that size. The baby's weight on the sixth was 4 pounds, 11 ounces, 2,126 Gm.).

While the growths were at their height, at 9 days of age, the child's blood count was: red cells, 5,870,000; hemoglobin, 102 per cent; white cells, 4,080; polymorphonuclears, 68.7 per cent; large mononuclears, 6.8; large lymphocytes, 12.3; small lymphocytes, 9.6; transitionals, 3.4, and eosinophils, 1. The only abnormality in the blood picture of this newly born infant was the leukopenia and relative increase in neutrophils.

* Submitted for publication, April 10, 1930.

* From the Department of Pediatrics, School of Medicine, University of Kansas. Biopsy material was secured by Dr. Earl C. Padgett, of the Department of Surgery; histologic examination of material was made by Dean H. R. Wahl, Head of the Department of Pathology.

Our first impression of these enlarged masses was that they might be due to an obstruction, such as atresia or absence of the parotid ducts. We soon became convinced from the position of the tumors that they were not intimately connected with the salivary ducts or glands. The mouths of Steno's ducts were open, and saliva was escaping. The mother gave her consent to the removal of one tumor, which was done through a small incision below the mandible, on the infant's thirteenth day of life. Dr. Padgett remarked that it popped out like a lipoma and seemed encapsulated.

Pathologic Examination.—The specimen was composed of irregularly shaped tissue, 23 by 13 by 6 cm., light yellowish-brown, with a few adhesions over the surface. The cut section revealed grayish-white cellular tissue divided into many lobules by fine fibrous septums.

The sections presented a very peculiar picture, there being masses of markedly lobulated fat tissue, separated from each other by bands of fibrous tissue. Many

Fig. 1.—Enlarged fat pads, outlined by tracing pencil, shown in a Negro infant aged 9 days.

of the fat cells were normal; others had cytoplasm that was vacuolated and often presented a foamy appearance. In other places, a rather grumose type of material was seen within the cells, a material which must take a basophilic stain. In other places there was considerable cellular proliferation between the fat cells, the boundary line between the fat cells and this cellular interstitial tissue being poorly defined. Nuclei were often numerous and arranged in concentric layers suggesting acinar formation.

Another peculiar feature was the presence of irregular lines radiating from the outer portion of the fat cells toward the center. Frequently, little cleftlike spaces radiating in the center suggested the presence of crystals that had dissolved out. Some of these cells were quite large. About some of these cells were a few nucleated giant cells, suggesting a reaction to a foreign body. The picture suggested a type of reaction resembling embryonic fat, but in addition leaving a deposit of lipoid or cholesterol-like material. In addition there was occasionally a mild inflammatory reaction about them.

Fat stains on this tissue showed a number of typical dark red masses in many of the fat cells that appeared normal. In some cells that had granular material and often were vacuolated, the fat did not stain so sharply but was paler, and suggested that it was either lipoid or some other type of substance which had a partial affinity for the dye. On examination with the polarized light, many of the clefflike spaces were seen to contain doubly refractile crystals.

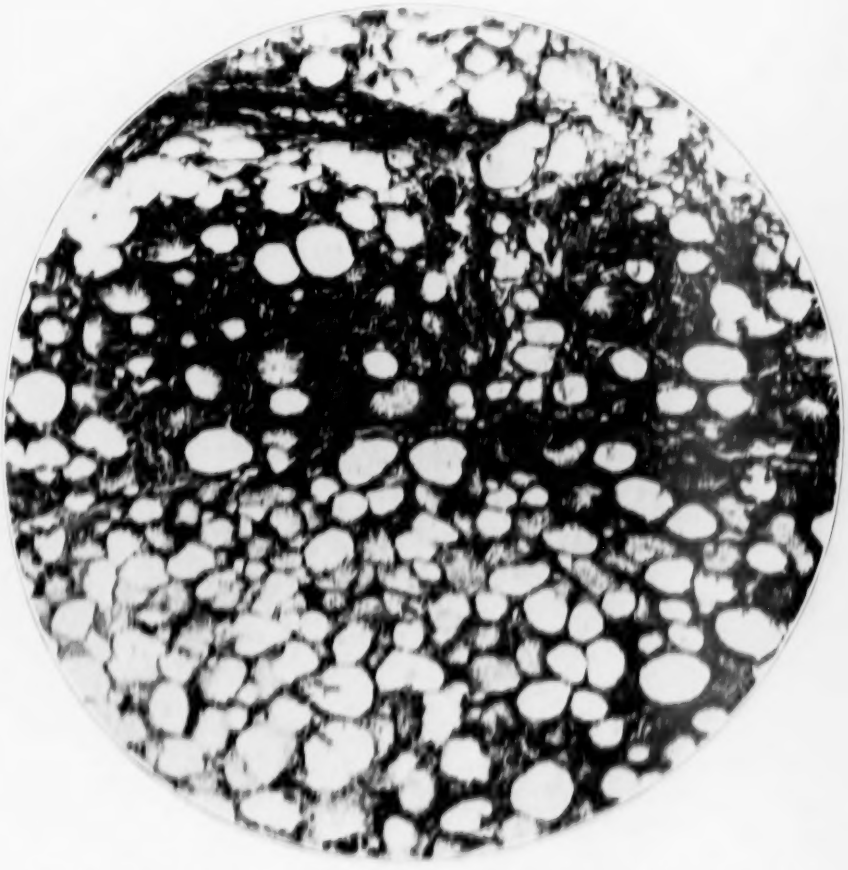


Fig. 2.—Section from sucking pad showing embryonal fat, lymphoid tissue and cholesterol crystals.

From the histopathologic examination of the section, the conclusion was reached that the growth consisted of lobulated embryonic adipose tissue, showing a mild inflammatory induration, probably an infection of the fat pad.

Although this disturbance occurred in adipose tissue, there was nothing about it clinically or histologically that resembled the manifestation found in new-born infants characterized by fat necrosis.

Subsequent History.—By the time the infant left the hospital on the eighteenth day of life, he weighed 5 pounds, 6 ounces (2,438 Gm.); the remaining pad was

receding in size and a few days later was not to be noticed. At 6 months of age he was well nourished and normally developed, and showed no evidence of the early disturbance; the cheeks were equal in contour and appearance, and there was no palsy of the face. According to the mother, there had never been any difficulty in nursing. A small scar under the right side of the jaw marked the site of the biopsy.

The corpus adiposum buccae or bolus of Bichat is described by Ballantyne as having the function of distributing air pressure and preventing the sucking in of "the cheek and buccinator muscles between the gums during the sucking act." The pad remains throughout the period of childhood and later. It is a body of adipose tissue, resting in the cheek wall beneath the facial muscles and fascia. Two excellent drawings of it are found in Scammon's contribution on the anatomy of infant and child. Usually the superficial portion of the fat mass is about 2 cm. in diameter. It is in the path of the parotid duct which is just above and toward the outside of the pad. Scammon [1] and other writers stated that the fat in this body has a higher melting point than that of most superficial fats. It is well known that the fat pads do not waste, even when other body fats are burned, in extreme nutritional disturbances and emaciation.

COMMENT

We have been able to find the record of a unilateral hyperplasia of the corpus adiposum malae in a 15 year old boy [2] and a few cases of lipoma limited to one side in children past infancy. We have been unable to learn of any report which mentions bilateral pathologic enlargement confined to the corpus adiposum buccae in the newly born child. Scammon,[3] as a result of his research on the development and fine structure of the sucking pads, found that at birth the pad is a structure particularly prominent in the well nourished child. In fetal life the growth in the first five months is principally due to increase in the number of fat lobules. In the later fetal months, the fat body grows because of the forming of new fat cells and the increase in size of the individual fat cells. Scammon stated that new fat cells stop forming usually by the end of the seventh fetal month, occasionally not until the last month.

In the case herein reported the infant was not robust at first, but was small, premature, and possibly affected by the toxic state of the parturient mother. The cheeks were not wasted. It is possible that

1. Scammon, Richard E., in Pediatrics, edited by I. A. Abt, Philadelphia, W. B. Saunders Company, 1923, vol. 1, p. 297.

2. Raffaele, Cecca: Iperplasia infiammatoria del corpus adiposum malae, Riforma med. **29**:1401 (Dec. 22) 1906.

3. Scammon, Richard E.: On the Development and Finer Structure of the Corpus Adiposum Buccae, Anat. Record **15**:267, 1919.

the fat pads continued to grow for the first ten or twelve days after birth, and at a rapid rate after the feeding and normal influences of growth were established. As a more plausible explanation, the finding of a mild inflammatory reaction in the biopsy material and the subsequent rather rapid decrease in the size of the remaining fat pad would suggest that the enlargement of these bodies may have been hyperplastic, due to a toxic influence.

Progress in Pediatrics

THE PSYCHIATRIC ASPECTS OF ENURESIS

FORREST N. ANDERSON, M.D.
LOS ANGELES

(Concluded from page 618)

COMMENT

PHYSICAL ASPECT OF ENURESIS

Race and Color.—The division into racial groups gives no important evidence. The relative dispersion among the various nationalities is what would be expected from metropolitan communities. There is no doubt but that some of the attitudes characterizing parents' treatment of their children have a partial root in the racial customs of the parents' own nationalities. But adequate tracing of this would be impossible in the scope of such a study as this, and one must conclude that nationality per se is not an important factor.

The same may be said of color. The ratio of 12:1, white to colored, is certainly not in excess of the ratios existing among the visitors to the clinics from which most of the material was obtained. I have been interested all along in any possible relationships between color and enuresis resulting from subtle conditioning factors. No worthwhile data on this have come to light, however.

Natal Conditions.—It is difficult to assign any definite causal value to the subject of illegitimacy. Since inferiority feelings appear in so many children in whom there is no questionable parentage, it can be assigned a rôle as only one of the factors in the production of these more directly causative inferiorities.

With five patients listed as of less than 8 months at the time of birth, it is permissible to speculate on inadequate neural development as a real factor. Weisenburg has repeatedly called attention to the likelihood of nervous symptoms among such premature children. By a perusal of the charts, it will be observed that postnatal development was usually retarded in these cases. No attempt is made to explain the 10½ months child; the facts may be otherwise.

As only 13 per cent of the enuretic children had a history of non-spontaneous births, whereas 24 per cent of the normal children had such instrumental deliveries, it can be stated definitely that the character of the birth is not a factor.

Postnatal Conditions.—It is interesting to observe that the figures for duration of breast feeding are six months or less for the normal children and eight months for the enuretic children. Various suggestions have been made by pediatricians on the possible relationship of prolonged breast feeding to subsequent infantile traits. I have discussed this question with Gilkey and Draney of Kansas City, who have had wide experience in children's training problems, but not primarily from the psychiatric point of view. There is thus corroborative evidence for this view.

As the comparative figures of development are studied, the following relation appears:

	Normal Children	Enuretic Children
Dentition	8	8—
Walking	13	14—
Talking	14	16—

Nothing conclusive can be gained from these figures; however, a slightly earlier value shows itself for the normal children.

No striking differences appear in the two groups in respect to the height-weight ratios; about one half of the enuretic children were of average height and weight, while 68 per cent of the normal children were in the same grouping. Deviations were not marked, except in a few instances.

Circumcision.—Circumcision has always been a source of discussion in all questions relating to the genito-urinary organs of male children. Information was not obtained on the control group, but among those with enuresis three-fourths had been circumcised. In a few instances this had been a recent operation, but in most instances it had been performed far enough in the past to permit any therapeutic effects likely to result.

Physical Inferiorities.—This topic requires careful consideration. For one thing it is the time-honored source of explanation of enuresis, along with almost every other "nervous" manifestation, and has found apparent confirmation in the numerous reported cures by physical means. This question was discussed in the review of the literature. It is observed in the present series that approximately 70 per cent of the children have either no detectable defect or defects of minor significance. It must be admitted that to declare positively that slight deviation has no significance is an impossibility, yet common sense and experience point to the very large percentage of all children who are deviates from the theoretical "normal." In this connection, too, there is the significant evidence of a series of consecutive cases from the Philadelphia Child Guidance Clinic in which enuresis was not a problem, although physical impairments rated high.

There is another element to the story, however, the importance of which can hardly be overrated. While it may not be the physical inferiority per se that causes enuresis, it may well be the attitude of the patient or the parents to that inferiority. Attention needs scarcely be called to the many cases in which the physician has coincided with the family in confirming the idea that this illness or that injury was the cause of persisting enuresis. Or it may be that merely a "nervous," "undernourished," "puny," etc., individual may exist and may be used as sufficient explanation of the trouble. There is thus easily built up in the child a "reason" which functions as a two-edged sword. In one way it serves as an alibi, relieving the child of the blame, and thus securing a relief from many emotionally depressing scenes, viz., scolding, teasing, whipping, etc. In another way it is a heavy weight, weighing down the child with its inevitableness and rendering useless any possible incentive to overcome the habit. For since it was caused by a physical thing happening or developing before the child's conscious life started to function actively, and is often beyond his control, it is of very little use to struggle against it. To be sure, this is not always the case, and in certain instances the believed physical origin gives the child something tangible to work on.

One of the most illuminating cases is that of Harry F., who suffered from enuresis since the age of 5 years, at which time he had suffered from a bite by a dog. Ever since then the physician and family had explained the enuresis on the shock of the bite from the dog, and Harry felt powerless at attempting the conquest of the habit. Under a procedure of explanation and reassurance, he proceeded to drop the habit rapidly and completely.

But I cannot escape the conviction that physical inferiorities do almost per se account for some cases. An outstanding example of this is the case of Howard F., a boy, aged 10 years, who started life under the handicap of a premature birth at 7 months. (Dr. T. H. Weisenburg has repeatedly called attention to the occurrence of neurologic observations in premature children, and the evidence is at least significant.) Sickly and retarded, he developed into an undernourished child with adenopathy, defective hearing, rachitic chest, fatigue posture, undescended testes and almost a constant dribbling of urine. The behaviorist can point out numerous conditioning influences, but even so these found their origin in the main in his physical underparity.

It would appear, then, that while no doubt exists as to the influence of physical factors, they are of much less influence than has generally been believed.

Illness.—Even if an exhaustive tabulation were carried on in this connection, it is not probable that much of conclusive value would be obtained. From the behavioristic point of view less depends on the ill-

ness itself than on the mutual attitudes developed between the child and the parents because of his illness. One thing, however, did concern me particularly, the occurrence of nutritional problems among small children in possible relationship to enuresis. Among the control children, only 6 per cent had presented such early nutritional problems; among the enuretic children, the figure was 30 per cent. This may be of considerable significance. But one must proceed cautiously in drawing the conclusion, for dietary, medical and economic factors are so different in these groups. Economic factors are probably less so than the others, for no correlation is observed between nutritional problems of childhood and financial status. However, even if the connection is not as direct as indicated by the 5:1 ratio, it is more than possible that certain common denominators exist in the children who are victims of enuresis and undernutrition. Is one of these common factors a physical underparity? Are the solicitude and anxiety engendered by one carried over to enhance the other? These and kindred questions present themselves with suggestive, but not final, answers.

PSYCHIATRIC ASPECT

Intelligence.—From this work develops a distinct impression that the average enuretic child is, if anything, somewhat superior to the average. Yet when one looks at the figures obtained in the intelligence quotient, this impression does not seem to be clearly borne out. It is there observed that the average intelligence quotient approximates 98, certainly not a superior group. But if a closer examination is made, some interesting observations come to light. Of all the known intelligence quotient values, thirty-one are above 110, that is, in the superior group, more than one fourth of all. And when the thoroughly legitimate elimination of those borderline cases has been made, this proportion is even more striking. And even with the inclusion of all, the number below 90 is only twenty-eight, or another one fourth. And on averaging these two subgroups it is found that those below 90 average 80, while those above 100 average 120.

These observations have been of unusual interest. They deserve some attempts at explanation. The situation appears about as follows: The intensity of emotional sensitivity has some correlation with the intellectual status, so that the brighter child early comes to regard his enuretic habit as undesirable and even shameful. This is less the case with the duller child. There is thus the setting for those emotional attitudes less desirable from the standpoint of cure—fear, shame, overconcern, lost confidence, etc. When I have discussed with various persons the subject of enuresis, it has happened more than a few times that a case has been cited, and almost always with the spontaneous comment that the child was more than usually bright and alert.

Handedness.—It is observed that in the known group 87 per cent were right-handed and 13 per cent left-handed. This is not greatly in excess of the normal occurrence of the latter condition, and probably does not warrant any clearcut conclusions. It is to be regretted that information on enuretic children is not as detailed on the early incidence of ambidexterity, for this would be of great value. But for clinic material naturally such knowledge is far less accurate than for the high type group constituting the controls. There it is noted that nearly one fourth of these control children give a history of early ambidexterity, becoming more set in the use of one hand as training proceeded. This in itself is of much interest to me, not directly along the line of enuresis, but as bearing on the question of such preponderance of control by one hemisphere of the brain.

Theoretically considered, left-handedness might bear some relation to enuresis by virtue of the psychic distress resulting from too rigorous efforts at replacing the right for the left as the predominant hand. On general grounds, there is some justification for believing that sufficient disturbance of the neuromuscular coordination may occur in such cases as to produce some interference with the elaboration of other neural paths, including those for the cerebral control of enuresis.

Specifically, only a slight amount of evidence for this is forthcoming; nevertheless, in a few instances one is probably justified in some such point of view.

Masturbation and Masturbatory Equivalents.—Throughout the psychoanalytic literature one finds mention of enuresis as a masturbatory equivalent. This may be an almost fully conscious erotic sensation derived from the frequent emptying of the bladder and thus the securing of a sexual satisfaction without the arousal of feelings of guilt. Or it may be a deeply unconscious substitution, and it is pointed out that at times masturbation commences when training for control of the bladder is started. Pearson has definitely found this to be the case in a case cited by him (personal communication). In this series it was observed that in a considerable proportion of the known children (63 per cent of boys; 30 per cent of girls) masturbation existed at the time they were under observation. These figures can argue in two directions. It must be remembered that the age of most enuretic children brought for study is well above the normal training age, and is within the period of frequent masturbation. A very high percentage of all boys give this history of masturbation, if one is to believe the statements of Moll and others. If this is true, the incidence of enuresis with masturbation is no more than one would expect in any group, and is explained on this basis alone. On the other hand, if enuresis is a real equivalent, one would be justified in expecting a definite lessening of the incidence of masturbation among

those who sought relief from enuresis. If such is the case, these figures are too high to be in accordance with the theory.

But one can argue on other grounds against the concept. In my experience enuresis is at the worst a highly disagreeable and embarrassing habit to the older child, but it is not, save in rare instances, one charged with an atmosphere of sin and moral degradation as is so often the case with masturbation. After a contact is established, nearly every patient admits an enuretic history; only rarely does he admit a masturbatory one; this applies equally to the children on whom this study is based and to the rank and file of patients interviewed over some years. It has not seemed that these two habits could be considered in the same light. From the standpoint of the psychiatrist or behaviorist, one may be no more "serious" than another, but from the more important standpoint of the individual they have been viewed as definitely in different categories.

As long as enuresis is viewed from the purely physiologic side, with sensory stimuli pouring in from the emptying of the bladder, there may well be much to this way of viewing the habit. It is rather from this standpoint of the attitude toward the habit that it appears contrary to a more common sense way of looking at it.

One must admit that there are significant associations in individual instances. The case of Evelyn is in point. In a girl, living under most unsatisfactory surroundings, including a sex experience with an adult male, enuresis, masturbation and sex play seemed to be the most outstanding characteristics, and careful study led to the conclusion that an intimate relationship prevailed between them.

Stealing.—As a form of malbehavior, stealing rates high in the causes resulting in study by child guidance clinics. It undoubtedly has deeply-lying mechanisms, discoverable in many cases. When a relationship exists between this and enuresis, it is often what one expects. When a child has stolen it needs no great imagination to visualize the psychoemotional upset resulting, and this is the fertile field for enuresis. But although several cases lend color to this view, the large group of children in whom enuresis is associated with stealing remains unexplained, since enuresis is a habit persisting from infancy, long antedating the other type of misbehavior. And yet these cases should afford unfavorable ground for the therapy of enuresis, when so much affective unrest occurs. So much for *a priori* reasoning; when one consults the tabulations, it is observed that several clearcut cures resulted when stealing was a major problem. To explain these, it is necessary to extend one's theoretical concepts, for in some of these cases the stealing was not materially improved, and one simply has to assume some continuance of the emotional unrest. But just as one knows how potently a major worry may eclipse a minor worry, or cause it to vanish, so one can see

here a major difficulty causing lesser ones to fall far enough away from the forefront to permit their disappearance.

Personality Traits.—Some attempt was made to seek data on the question, "What manner of child is this victim of enuresis?" To describe these characteristics adequately is entirely beyond the scope of this paper, but some worthwhile impressions backed by certain statistical data are forthcoming. Certain traits are discussed in much more detail.

Two thirds of all those concerning whom suitable information was obtained were rated as unusually timid. Criteria and opinions vary widely, but even so, this is a high percentage. The enuretic habit, with its attendant shaming, may in no small degree have been responsible for this.

Sensitiveness is a trait of even higher incidence than timidity, and was noted in 70 per cent of the patients. This is significant, although it is possible that sensitive children are products rather than causes of enuresis. In fact, the interrelationships of this kind are exceedingly complex, and no attempt is made to separate them. But the fact of some relationship is clear and must be considered of importance.

Aggressiveness is an uncertain observation, since less information was obtained on this than on other traits. However, on the basis of the data 60 per cent of the patients are reported as aggressive. To harmonize this with the high incidence of sensitiveness is difficult, but it is noted that these figures apply to a total of only one half of the patients, and among these they often coincide with those listed as either nonsensitive or indeterminate. To this extent it is a situation that is not comparable to the sensitive group.

Slightly over one half of the patients are considered reasonably good misers, although, as mentioned elsewhere, this group is made up of those who could not better be classed as seclusive.

Jealousy was found in 60 per cent of the children who were observed for this trait. While it is believed to be an important factor, it is considered in more detail under the heading "Relationship to Siblings."

Infantile Traits.—The case tabulations show a large percentage of patients classified as infantile. Before this designation is applied, several points are considered. In the first place, one must search the records for definite statements by the examining psychiatrist or psychiatric social worker that the child was so considered with this in mind. It may well be that in some cases the designation was applied on an insufficient basis; nevertheless, all emotional traits are as yet in the stage of impression rather than mathematical fact. In the second place, one should adopt certain criteria of determination of any particular trait, and it is believed that nowhere does this necessity lie more deeply than in the broad term of emotional infantilism. Much thought and dis-

cussion over this subject have led me to feel that the following characteristics may be evaluated in designating a child as infantile: (1) the ease with which a child yields in his attempts at solving any problem, or, stated otherwise, his lack of persistence; (2) the ease with which he is reduced to tears; (3) the nonassumption of responsibility suitable to his age, and (4) the tendency to be swept into profound changes in mood by trivial things.

In every one of these it is obvious that full cognizance must be taken of age, for to compare the activities and moods of 5 and 10 years, for example, is manifestly unfair. But if one constantly holds in mind the probable normal or average behavior of a child of this given intellectual and chronological age, a fair comparison may be made. At first thought it would seem that consideration must be given to environmental factors that have helped shape behavior, but further study shows that these are determiners of the infantile behavior and not the measures of it. In the third place, it has become more or less tacitly accepted that certain common behavior modes are infantile. Probably foremost of these is the tantrum, and with such definite criteria one may be reasonably safe in describing a child.

It is unnecessary to cite individual cases in this connection, as such a large number fall in this category under one of the criteria discussed.

"Temperamental Traits."—The use of this term as a separate characteristic needs some explanation. It is one of those words with which every one is more or less vaguely familiar, but which few can use accurately. Early in my studies on enuresis I was confronted by the statements of the heads and assistants of institutions, that many of the children with enuresis were "temperamental." Gradually it became interesting to search for evidence of this, either by direct questioning of those who knew the child best or in the records of the examiners. Surprisingly often positive replies were forthcoming. No real attempt is made to define it—after consideration it has been left as an autonomous term, although there is a clear realization that it signifies different things to various observers. Often the question was asked: "What do you mean by 'temperamental'?" And out of it all came the concept of an unstable equilibrium in the emotional sphere. Probably in some instances other meanings would be nearer the truth, yet emotional instability is a broad term, of some value, which characterizes moderately well certain emotional manifestations.

On the basis of such criteria it is interesting to note that three fourths of all the children with ascertainable information on this point could be so characterized. In spite of its vagueness, there is much inclination to regard this as one of the most definite observations of the entire study. If a large percentage of enuretic children are emotionally

unstable, it may well be that casual relationship exists between the two. It does not follow, however, that emotional instability is the etiologic factor, or even one of these, for it is probable that instability is accentuated by persisting enuresis. But this is the situation in many psychophysical correlations, such as the "thyroid-emotion" interplay. To establish a mutual relationship is of no small worth, even if antecedent and consequent cannot invariably be determined. Case histories have to be taken in toto to afford valid evidence in this relationship; as one reviews the personality studies of many children, evidence of unstable equilibrium in the realm of the emotions comes into view. And it is on this basis that the high percentage indicated is determined.

Depth of Sleep.—For several reasons it is difficult to gather clinically accurate data on such a question as the depth of sleep. In the first place, unless unusually pronounced, very little attention would be focused on it, unless there was occasion to awaken the child frequently. So that of two children equally difficult to awaken and only one having enuresis, the matter would demand attention only in this one. In the second place, there is the more or less unconscious desire to create an alibi in defense of undesirable habits in one's children, so that this reason, functioning as an excuse, is often given. Approximately one half of all the children with sufficient information to warrant an opinion could be classified as deep sleepers. Since the law of probability can obtain here, this topic must be dismissed with the conclusion that no certain evidence accrues to justify consideration of enuretic children as especially deep sleepers.

Inferiority Feeling.—Nothing has attracted more popular attention, to say nothing of concern by psychiatrists, than the feelings of inferiority, generally referred to as the "inferiority complex." To determine something of its prevalence among the children of this study seemed interesting, although of doubtful value. For one thing, as in all personality characteristics, it was more likely to be effect than cause. For another thing, it can be predicated in some form or another in practically every case, for even the superiority complexes are viewed as maskings or compensations for underlying deep felt inferiority. However, one of the real purposes in studying enuresis was to ascertain what personality influences it might have on other life activities of the victims. The incidence of inferiority feelings based on evidences or opinions of some well qualified observer is remarkably high.

While obvious inferiority feelings undoubtedly preponderate, in a certain small number definite feelings of the opposite type, e. g., superiority, are to be observed. These may be noncompensatory, in the sense that they are natural consequents of attitudes of the parent. Thus in Fitzthomas S., a colored child, aged 7, much of the behavior difficulty

was attributable to his superiority complex over his West Indian lineage, considered by his parents to be far above that of American negroes.

Whatever the direction of the pendulum, the swing in these connections is away from the emotionally balanced personality and as either cause or effect is of marked importance. Viewed in the light of studies made on enuresis, I am led to wonder seriously about a very close friend, who is known to have had enuresis until almost beginning adolescence, and who has always suffered from inferiority feelings. He has no assurance that there was a causal connection between the two phenomena, but it is at least highly suggestive.

Parental Maladjustment.—One would have much temerity to argue directly for the special influence on enuresis of poorly adjusted parents. When looked at closer, nevertheless, an undoubted indirect relation is seen to exist, so great that nearly two thirds of the homes from which these enuretic children came manifested such maladjustment. If it is the child subject to emotional tensions that suffers from enuresis, then certainly such causal factors occur more often in poorly adjusted families. If attention is directed to a few specific cases, this may be seen: (1) James N., a child of highly educated parents, suffered from marked maladaptability over the mother's intense desire to continue outside work. This was opposed by the father, with the gradual development of the point of view by the mother that her child was the innocent cause of her thwarted ambitions.

(2) Helen B., the child of mutually infantile and disharmonious parents, battered by one side and then by the other, found some outlet in a multiplicity of undesirable habits.

(3) Irma R. was the adopted child of a hyperrationalizing father and an infantile, dependent mother. Undoubtedly she came to represent to some degree an emotional outlet for the foster-father, deprived of adult relationship with his wife. (4) C. A., an unhappy boy, lived with parents who were never really adjusted to each other. He constantly heard himself likened to his father, a comparison that was anything but complimentary. Probably this was the one really important factor in this case. (5) Edith C. was brought up in an atmosphere rendered unhappy by pressure of the father's family to compel the mother to change religion. Likewise, definite sex maladaptation existed between the parents.

(6) Joseph F., whose parents lived together until he was 5, but with almost constant fighting and quarreling, ceased his habit under relief from this strain. (7) Virginia R., aged 6 years, had good intelligence and a winning personality. Associated with her enuresis was masturbation, the real cause of reference to the clinic. As the study went on, it became evident that the real difficulty was between the father and

step-mother. Gradually the former poured out his troubles, receiving reassurance and kindly sympathy from the psychiatrist, and as he obtained relief, the child, released from the home tensions, ceased her undesirable habits in a definite manner.

Many other cases could be cited. It cannot be stated what the actual connection is in many instances, and probably there is no such connection in some, but in others the home atmosphere is clearly basic to the child's emotional disturbance.

Parental Attitude of Failure.—Not the least of the emotional factors involved in this complex habit is that having to do with the "expectant failure" attitude of the parents. No evidence needs to be marshaled for the worthwhileness of the attitude of confidence and success; indeed it is almost axiomatic in the proverb that "nothing succeeds like success." Elsewhere it is discussed on the more positive side, but it seems well to mention several instances in which an outstanding element in the situation was the placid resignation of the parents to a supposedly inevitable thing. A boy, aged 8, and his sister, aged 5 (Gilbert and Thelma L.), had suffered from persistent enuresis. As various remedies had been tried and had met with no success, the mother had become convinced that nothing could be done and had patiently conveyed this idea to the children.

The mother of Edith C., aged 4 years and 6 months, had half-heartedly tried many things, only to adopt an attitude of inevitable failure. Such a negative attitude, while to be deprecated, nevertheless, has something in its favor as opposed to the severely condemnatory actions of many parents. At the worst, the child suffers from a sense of inevitability, but such a sense can oppress him well nigh as acutely as the conscious sense of guilt attendant on the other method.

Religion.—Not the least of the indirect factors causing emotional unrest in children is parental disharmony over religion. In a larger sense this factor falls under the broad heading of parental maladjustments and is discussed only briefly. But several cases bear eloquent testimony to the devastating consequences on the child of parents quarreling over this topic. Often it involves other family relationships, the interference of grand-parents, etc. And since these quarrelings are often precipitated over the question of the religious disposition of the child, the child does in fact become both a cause and a result.

The case of Edith C. is such a one. Reasonably satisfactory adjustment was effected until the question of raising the child in the faith of her father came up. Ultimate submission by the mother occurred, but with it came inadequate compensatory adjustment and seclusiveness, all of which combined to exert a detrimental influence on the child. Irma R., the adopted child of an atheist and of a rabbi's daughter, was

brought up under the emotional tension bound to result between such dissimilar parents.

Economic Status.—It is a certainty that enuresis is a visitor in the families of every economic range. The series shows a majority in the lower strata on the financial scale, but the conditions governing all clinical material can entirely account for this. From certain angles, indeed, the pampered and emotionally unadjusted child of the more wealthy family is more prone to continue this habit than is the case with the child in the large family of lesser means.

In the latter instance, so frequently other more pressing problems demand attention, with the result that enuresis ceases to occupy the foreground and is thus given more opportunity to fade out. On the other hand, in certain of these families it is so injudiciously considered as to bring only physical punishment and intense scolding. Between these extremes range every possible variation, and it can be unqualifiedly stated, as a result of this study, that enuresis as a general problem cannot be considered as largely influenced by the economic factor. Individual cases do present, however, the imprint of economic influence, and often it is felt that were money available to provide a different environment much might be accomplished.

Evelyn G. had a father who had struggled unusually hard for supremacy to avoid feelings of social and financial insecurity; as a result, he had become extremely intolerant of social lapses in his family. He considered enuresis as a lapse, and one can easily feel that were economic security guaranteed him, it would be much easier for him to avoid the painful pressure he applied to this child for her habit. Helen B. found so little of both parental harmony and economic security at home that she fell back on numerous childish modes of gratification, of which enuresis was one. John S. suffered from a paternal insecurity almost identical to this; his enuresis was the source of intense mortification and emotion by the father. Jacob H. had a violent tempered father and a harrassed mother woefully depressed over poverty. The psychiatrist felt that low economic standing was a direct influence.

Numerous cases might be cited on the more obvious effect of lack of money; it has been deemed of more importance to note certain indirect effects. Illustrations of the other type—in which abundance of money has but rendered the child more infantile than otherwise—are not necessary.

Relationship to Siblings.—When attention focuses on the relationship of the child with enuresis to other children in the family, the illustrative case material becomes legion. About one half of the cases seem to show this influence. This runs the gamut of almost every

conceivable relationship, from infantile dependency to acute jealousy and antagonism.

Donald E. was the youngest child of a large family. One had only to talk with his mother for five minutes to realize how truly he was babied by all the others. At times his abortive attempts at self-assertion caused him to desire to change places with the older sister, but the childish demands were too strong, and he relapsed quickly into an admission of desire to be the baby. James Q. likewise had been the recipient of much "maternal" solicitude on the part of his older sister over his enuresis and soiling. At the same time he had suffered severely negative comparisons with his younger brother. While apparently these emotional forces are opposed and should neutralize each other, unfortunately the destructive component of each has been the effective one.

Joseph D., aged 13 years, constantly had held before him the superiority of his brother, and could hardly fail to see that his main worth to his mother was the money he could earn. An illegitimate child, it is noteworthy that his mother's repeated subsequent pregnancies were always associated with exacerbations of his enuresis and malbehavior, furnishing strong evidence of the mental attitude built up in him toward siblings. Charles A. suffered acutely from the disgusted expression and shaming inflicted by his younger sisters. Lewis A. was a remarkably bright youngster, who, finding that a younger brother usually won out in their fights by virtue of the mother's interference, soon learned that enuresis, while not winning favorable comment, at least attained attention over that given his brother. Fred W. had seen a younger brother steadily favored, thus encouraging in him the growth of jealousy. Mary H., aged 7, had developed clearcut feelings of inadequacy and social inferiority through too much companionship with a more gifted younger sister.

Habit Training.—It will be noted in the tabulations that defective habit training stands almost at the head of the list in the factors in evidence in enuretic children (87 per cent). Looked at one way this may seem an overstatement, for it must be freely admitted that one could find some fault in any family under observation. On the other hand, such obvious faults appear in many cases, faults which the trained parent might well have avoided. In many cases this habit training would seem to be the main difficulty—inconsistency in dealing with desirable habit formations. Usually other factors enter, and it becomes a sheer impossibility, in the present state, to determine accurately the influence of any one.

Often it is a case of the mother inflicting on her child the results of her own neurotic childhood. Thus, Doris D. was the child of a mother who was an only child and intensely dependent on her mother.

It is not to be wondered at that she developed in her own child the same dependency traits, actually opposing the growing up processes. Nor is it surprising that illnesses play such a destructive part in consistent habit training. A regimen may move on satisfactorily for a time, and then may be broken suddenly by the appearance of illness. It requires unusual firmness to pursue a systematic course under such conditions, and it may often be completely impossible. Then the illness passes, and the endeavor is made to reestablish the habit regimen. The child opposes, and falls back on the bulwark that proved so effective, complaints of illness. They may be real, but they probably are not; the mother errs on the side of sympathy and the reestablishment of training rapidly becomes increasingly difficult. Often it is given up in despair.

Here, too, enters the full force of the conditioned stimulus-response idea, to be discussed. If a single incident can stop or start a habit, it is seen how incessant is the watchfulness necessary to maintain the path of training.

Conditioned Reflex.—The subject of the conditioned reflex has found its way abundantly into the literature in the explanation of countless habits. Whether it is the same in principle as the time-honored "association of ideas" can hardly concern one here. Whatever its real nature, primarily neural or psychologic, it serves admirably to give an understandable picture of what occurs in many instances. In this field of enuresis it finds its chief function in the explanation of cases in which habit was rather suddenly reacquired after a period of freedom. (Since about 17 per cent show the development of enuresis after infancy, it is significant that sixteen children showed such a conditioning factor.)

A number of illustrative cases are given: Mary C., aged 13 years, was brought up by an aunt, as a member of the family. At the age of 12 a severe and permanent illness of this aunt necessitated the placement of the child with another aunt, a procedure which was natural enough in itself, but which must have impressed the child as a peculiar selective action, as none of her supposed siblings was removed from the home. At this time she contracted a cold and commenced wetting the bed, a habit she had not had since infancy. This habit continued in the new home, where her cousins were of a definitely superior intellectual status.

Howard S. had secured control in his earliest infancy, but at 15 months was greatly frightened by the sudden appearance of a stranger in his room. This was followed by enuresis and other infantile behavior, repeatedly securing for him permission to get into bed with his mother.

Joseph had secured complete control over the enuretic habit for a matter of many months. Then occurred a party at which watermelon, ice cream and lemonade were served. Naturally he suffered from incontinence that night, with a complete return of the habit. It is a striking illustration of a physiologic stimulus conditioning a habit, when associated with sufficient emotional stress.

Marian D., a colored girl, aged 10, had secured control before the age of 2. At the age of 2½, she was placed in a foster-home in the country and suffered from neglect. After being left on a cold porch, she suffered from severe pyelitis and developed enuresis; since then she had opposed any attempt at conquest of the habit, by accusing her mother of neglect at that time. Similar to this is the case of Everett D., whose mother left him exposed, presumably under a physician's instructions, so that he became ill. He acquired an antagonism to his mother, manifest in part by enuresis, which habit promptly cleared up when he was sent away from home to a boys' camp.

Institutions.—If the twenty-six children resident in institutions are excluded, only eleven children had been institutional residents. What influence this may have had is doubtful except in one or two instances. The case of George is that of a youngster held in a Home far beyond the usual time, becoming a "pet" of the caretakers and receiving conditioning influences rendering outside adjustment more than usually difficult. Institutional life in relation to enuresis is discussed under the heading "Enuresis as an Institutional Problem."

Foster-Homes.—Eighteen children resided in foster-homes. It was never possible to determine any especially direct relationship of this residence to their enuresis. However, it can easily be seen that a less secure existence usually obtains in the foster-home, in that too undesirable behavior often results in rejection, a reaction much less likely in the child's own home. The case of David B. was in point. He had been in three or four homes successively, losing out in each because of his enuresis and soiling. Such a state of affairs could not make for stability, and no results worthy of mention were obtained. Several others appeared to be in essentially the same status. Again I come back to that conclusion: Whatever is the cause of the enuresis, its persistence is almost directly proportional to the emotional stress and insecurity. Foster-homes are almost certain factors in this insecurity, and in that way are important factors in a group of enuretic cases.

TYPE, ONSET AND STATUS

Type.—Approximately four fifths of all cases studied were of the purely nocturnal type. This is the more understandable variety, since the possibility of failure to gain cerebral control over spinal centers

can be appreciated by the most intelligent persons. About 11 per cent were of the combined nocturnal-diurnal type; less than 4 per cent were of the purely diurnal enuretic group, while 7 per cent had combined enuresis and soiling. The last named group is the hardest with which to accomplish results. I worked on four of these cases, and had a rather depressing feeling of failure in three. It is believed that these children have been subjected, by their habit, to far more disturbing influences than those accompanying enuresis. The latter may often escape detection, even when diurnal, and it is not the socially disgusting habit which is the case in lack of control of the bowel. As a result, the only defense possible for the victim is complete acceptance of his condition, and this easily leads to absolute loss of confidence. In two of these children no real endeavor could be elicited.

Diurnal enuresis, although less depressing to the patient, likewise brings more parental and group condemnation than does the nocturnal type. On the other hand, it is something toward which effort can be tangibly directed by the patient. In the sufferers from both types, it was more than interesting to observe that what usually first disappeared was the nocturnal type. The case of Norman S. was an excellent one in point. Although marked improvement resulted, it was easily more evident in the nocturnal variety. His punishment and scoldings were largely for the diurnal manifestation, and naturally it was this on which he maintained a firmer hold—in spite of conscious desire to the contrary. In fact, these observations were among the strongest confirmatory evidences for the psycho-emotional influences on enuresis.

Frequency.—Very little can be added to the simple figures on this topic. So far as could be determined or estimated, the average was about five times weekly. It is probable that this is higher than would occur with the general rank and file of enuretic patients, but when parents come for assistance usually the difficulty is a frequent and pressing one; hence the high figure. Further, a large number, thirty-four in all, gave insufficient data on which to make a reasonable estimate. This group coincides largely with that in which enuresis was not the major problem for reference to the clinic.

Onset.—Just over 80 per cent of all known cases show the origin of enuresis in infancy, with its simple continuance beyond the age of babyhood. These are the more easily understood cases, at least superficially, for it is the persistence of a well formed habit into a period when adults do not accept it as kindly as they do earlier. It is with the other group, however, that more interest attaches. Why should certain children recommence a habit long after it has ceased? This is closely associated with the influence of conditioning stimuli; in every case an earnest attempt has been made to ascertain what may possibly have

caused the recurrence. In some it was undoubtedly illness, with a physiologic basis and the creation of a psychologic "setting" suitable for its continuance. If one neglects the cases occurring before the age of 3 years, which is accepted as the upper limit of normal, it is noted that twenty-one show enuresis recommencing after a period of complete freedom. Fourteen of these, or two-thirds, present such probable precipitating causes. These are more fully discussed under the heading of "Conditioned Reflex."

Status.—What was accomplished? After all, if the ultimate value of any method or, indeed, of any scientific fact is the results it produces, one is justified in asking what results were obtained here. With that an examination of the situation in this respect is in order. In such an analysis it is always possible to find reasonable alibis, and it is necessary here to do this to some extent. These cases represent a series drawn from diverse sources; I could not study many personally and many could not be seen frequently or for a long enough period of time. But with all reservations, one common denominator remains—these cases were not subjected to drug therapy; all effort was along psychotherapeutic and "routine measure" lines.

Approximately one-fourth (23 per cent) were considered cured. This means complete cessation of habit for a period of at least ten times the preceding average interval, except for a few exceptional cases in which accidents did occur. It became obvious early that to hold the criterion of cure as being absolute, immunity would be an impracticable and impossible ideal. Even if a child did not have enuresis for ten months (the maximum observed personally) no guarantee could be given that he might not have an enuretic episode, and if such were to occur, was it to throw this child out of the "cured" group? Technically it would do so, but it would serve no practical purpose. What is desired is a working assurance that a given child has conquered his habit, either completely, or so nearly completely as to permit him to function as a person without enuresis. It is realized that this point of view is open to criticism, yet it is what is done regularly in many kinds of medical practice, and it was the only point of view serving a workable purpose. If a youngster had been wetting the bed three times a week, and came, after three months' work, to a place where he had an accident once in two months and then went on again with no further enuretic history up to the time of cessation of the study, say two months, that child would be considered cured.

Improvement, reported in 34 per cent of additional cases, is an inappropriate term. Again it is open to a wide range of interpretations, a very liberal one permitting well nigh every case to be so considered. But practical results must be used as criteria—if a child dropped from

a frequency of five times a week to twice weekly he could be regarded as definitely improved.

Under these interpretations, then, 57 per cent of all cases resulted in cure or definite improvement. No alteration occurred in 15 per cent, while the remaining 28 per cent either were lost to view before results were obtained or for some reason were impossible of satisfactory classification. These figures do not present as decisive results as do a few of the reports in the literature, yet I am convinced that after all legitimate deductions have been made, the percentage of improvements and cures, based on a frank but simple psychotherapy, cannot but be considered as strongly confirmatory evidence for the affective basis of many cases of enuresis.

ENURESIS AS AN INSTITUTIONAL PROBLEM

That this habit occasions no end of worry to institutional chiefs and caretakers is learned very early in the contact established with such institutions. It presents a moderate economic problem in the way of excess laundry; it proves irritating to those having children in charge, so that its effects are radiated far beyond the problem itself; it raises problems of discipline, and it exerts, above all, a destructive influence on those subject to it.

Institution A.—This institution houses about twenty boys and ten girls ranging in age from 5 to 12 years. Each group sleeps in a single large dormitory, in single beds. Lights are burning in the hall, but are not left on in the bathrooms, which are only about 10 feet from the dormitories. The boys and girls play together frequently and occasionally are permitted to go out, with the inculcation of a sense of responsibility in the boys. Freedom of expression obtains, and it is believed that a genuine affection for the home and matron exists. Traces of severe and harsh discipline under previous administration come out in talks with the older children.

Enuresis is limited almost exclusively to the boys here; the reason cannot be ascertained. Four boys suffer to a considerable degree. A large amount of teasing results, yielding definitely sensitive reactions from the older enuretic children, with little apparent response from those 6 years old. A free tendency to inform on others exists, but it is noteworthy that among the older boys a genuine endeavor to help the enuretic children often obtains, in that they will often arouse these youngsters. It is the matron's opinion that altogether too much stress is laid on the subject, that eventually it is a disappearing habit, and that the less emotional strain developed the better.

Institution B.—This is a home for colored girls—orphans or unhappily housed children, ranging in age from 3 to 16 years. A minority

presents "difficult" or behavior problems; the mentality in most cases is "pretty fair." The children attend a public school, being transported by bus. They reside in two practically independent cottages, between which a spirit of friendly rivalry is gradually developing.

Of a population of thirty-six, an average of about five have enuresis. It is the matron's impression that enuresis prevails more among the lower intelligence group. In the younger children a fair degree of success has been attained; with the older ones, less is accomplished. Practically no cases have existed in which the physical condition could be considered definitely as causal. Routine treatment consists of either awakening the children or taking them to the bathrooms at about 10 p. m. After that no definite routine is followed—sometimes some will be awakened.

It is not felt that the enuretic children can be characterized as excessively deep sleepers. They might be grouped as the "heavy, slow, phlegmatic" type. Nor has the matron observed a close correlation of enuresis and other infantile characteristics. Particularly does she feel that sex play and masturbation are not contributing factors, since a procedure of utter freedom of discussion has been devised here. Older children wash their sheets, with the definite idea in mind that it is a natural consequence of the habit and not a punishment. Nevertheless, the older girls not afflicted tend to assume an undesirable attitude toward this and that this is a large factor.

Institution C.—This is an orphanage housing fifty-five children and usually having six or eight cases of enuresis, almost always among the boys. Considerable conversation with the matron of the cottage having the largest percentage of enuretic children revealed some helpful understanding of the problem, in the way of avoidance of physical punishment and cooperative attempts to solve the problem. However, the old idea of enuresis being caused by masturbation was tenaciously held, and had been used in explanation to the boys. Attempts at working out card charts, with reassurance, produced some really favorable results; circumstances prevented adequate intensive work, however.

Institution D.—This institution represents a semireformatory type, where boys were placed either on court order or pending more permanent adjustment. A number of visits were made to this home, and real cooperation was given. However, an individual study was not made. For one thing, past records were necessarily inadequate, and in no case could it be determined accurately when or why the enuresis commenced. Effort was restricted to making some group observation on this type of boys, together with much discussion with the superintendent, a woman who had had a long series of such youths pass under her direction. The morale was good, and something approaching a

collective spirit was evident. Boys were never punished for enuresis, although usually some attempts were made to arouse the worst offenders in this respect sometime before midnight. It was this matron who first suggested to me the idea that enuresis is more frequent among "temperamental" children.

HOSPITALIZATION

An interesting phase of this investigation relates to the effects of hospitalization on the enuretic habit. The object of such residence in a hospital was, of course, twofold: the determination of any possible physical or neurologic basis for the habit and the observation of results obtained from certain planned procedures.

In the case of four boys, it was possible to obtain an exhaustive study, from every reasonable point of view. Joseph F. was hospitalized at the Pennsylvania Hospital for Mental and Nervous Diseases for slightly more than two months, October and November, 1927. From a perusal of his chart it was seen that there had been a great deal of disharmony in the family, resulting in separation when the patient was 5 years of age. He had always had enuresis, but after satisfactory placement in a foster-home had given no evidence of this condition for some weeks, until a children's party at which large quantities of watermelon and ice cream were served. That night he wet the bed, an occurrence that reprecipitated the old habit in all its force. At about the same time he developed severe tantrums after learning that such behavior won for him certain privileges with his foster-grandfather, of whom he was quite fond. In addition to all routine tests of physical, neurologic and laboratory nature, his urine was subjected to repeated tests for night concentration. These results were uniformly normal.

During his stay in the hospital, he mixed readily with the boys of the "behavior group," and the enuresis soon completely ceased. No other treatment was instituted. He was discharged as cured to his former foster-home, and reports some months later gave a negative history for enuresis.

It is felt that the early development of inferiority and insecurity feelings had created an infantile and dependent attitude. There was also the obvious influence of a physiologic conditioning factor. Given association with a group of equals, he readily dropped his infantile behavior, not only enuresis but the tantrums as well.

Jerry N. was likewise hospitalized for nearly two months at the same institution. His early history was of marked parental bickerings and unhappiness. In addition he labored under the handicap of encephalitis, with its attendant train of awkward musculature, sluggish pupils, etc. In his case enuresis had commenced at the age of 9, two years before, but not until some time after the encephalitic attack. His

career with the boys of the hospital was not promising at first—he was in effect rejected—and meanwhile no improvement was observed in his habit. Laboratory and concentration tests gave negative results, as did roentgen examination of the spine. Gradually he became a more accepted member of the group, and coincident with this came great improvement in the enuresis. No treatment was instituted except to provide for his regular micturition each four hours by day. At the end of about two months he was discharged, with a subsequent report that he was almost cured.

James O. was hospitalized at the Orthopaedic Hospital for almost two months. His early history was of paternal ill treatment and family discord, coupled with much shaming by contrast with a younger brother. James had soiling and the diurnal as well as the nocturnal type of enuresis. All tests gave negative results, including concentration tests and roentgen studies. He was given individual psychotherapy by myself and by the nurses, who cooperated excellently in the work. Throughout his attitude was that of mild interest, but more because of the attitude of others than from an intense personal desire to conquer his difficulties. Improvement was rapid, and for one month was practically perfect. He was aroused regularly at night, but all other responsibility was put up to him. After discharge he maintained his good record for a time, but soon drifted back into the old regimen under the influence of home and school surroundings. It was felt that the fundamental difficulty in this instance was the impossibility of ever getting into a vital contact with the youngster. His desire to please was so irritatingly present that never was there aroused a real incentive from within himself.

Donald E. was studied for two weeks at the Orthopaedic Hospital. All studies gave negative results, with the exception of the concentration test of the urine, which demonstrated some functional incapacity on the part of the kidney to heighten the specific gravity at night. His history is almost ludicrous in the evidence of babyishness. The parents and older siblings alike combined to hold him in the emotional bondage of infancy and to expect him to emerge from this was to expect the impossible. He showed improvement in the hospital, but this could be accounted for largely on routine awakening. Nevertheless, he did show some later improvement, under a fairly consistent routine at home of awakening during the night.

These four boys constitute those on whom it was felt that complete studies were made in a hospital. Certain additional cases afford indirect evidence of the possible effects of hospitalization. A striking illustration of this is the case of Elizabeth H., detailed in the account given the "H. family." In the histories of several children occur accounts of temporary residence in hospitals for other purposes, and almost

uniformly marked diminution or complete cessation of the habit occurred while in such residence.

Although the cases are few, it is believed that the results justify some definite conclusions on this subject. All cases are evidential against the influence of discoverable physical defects. To be sure, the fourth case did present a functional disability of the kidney, but even if based on a real structural defect there are such obvious additional factors as to render this unlikely as the sole etiologic element. In the second place, it must appear of the greatest interest to observe the influence of mere change of residence and routine, without specific treatment. This is of double significance when consideration is given to the unsatisfactory emotional status existing in the home life of each child. And lastly, in the cases of the first two boys is noted the apparent influence of gaining a place with the group; as soon as this is accomplished, childish habits drop away and remain in abeyance after a return to previous surroundings.

THE H. FAMILY

One of the most interesting subgroups studied was the H. family with four children, all of whom suffered from enuresis.

The father was a lazy, shiftless person, never affording an adequate support, changeable in disposition and arousing more fear than affection in his children. The mother was a fairly intelligent, cooperative woman, brought up in an extremely repressed home, utterly unused to the way of the world, and very soon thoroughly disillusioned by her marital experiences. She was eager to avoid for her children some of the pitfalls occasioned by her own ignorance. The father had enuresis until the age of 17; he had a brother who had suffered from it until the age of 16. The mother had had difficulty with micturition ever since marriage. This had led to a general belief in the family that enuresis was an inherited trait.

Mae, the oldest girl, aged 12, was dull appearing, fearful and given to tantrums and fought vigorously with her father. She had had enuresis since infancy, but it had been much worse since a severe scalding at the age of 2½ years. She was very self-conscious of her habit; she was usually awakened by the first appearance of urine and arose immediately. Her intelligence quotient was 90, contrary to the lower estimate of a psychiatrist. Anna, aged 10, had a mild cardiac condition and was definitely undernourished. Her intelligence quotient was not determined, but was estimated to be about 90. She had had enuresis since infancy, almost every night; she was a deep sleeper. She had much less concern over the habit than her older sister. Elizabeth, aged 8, was a rather dull appearing child, from whom little could be gathered in conversation. She presented a pronounced instance of mirror writing alternating with normal writing. Enuresis had been present from infancy and averaged six nights weekly. Jack, aged 6, was a fairly normal appearing youngster, on whom no study was made. Apparently he was more or less naturally following the path of his sisters.

At the same time that the oldest child was brought in for examination, the third child entered the hospital for a tonsillectomy. While there she awoke from a dream very much frightened, fearing that she had urinated in bed. On finding that she had not done so, she called for the nurse and thus passed the night dry.

On returning home she repeatedly reported the recurrence of this dream—that she was in the hospital where it would be a terrible thing if she should wet the bed, and invariably she would awaken, so that after a period of three months there had been no relapse.

Meanwhile, Mae was given massive doses of reassurance by the staff at the clinic, with the result that almost at once enuresis diminished and within three months' time only one or two very slight accidents occurred. Ann likewise almost immediately commenced having a dry bed, even before she was given any treatment. It would seem to have been a case of psychic contagion; with the sudden and dramatic disappearance of the habit in her older and younger sisters, there was seemingly nothing to do but to fall in line.

As to the fourth member, the boy, although some improvement had occurred, opportunity for study was not available. Unfortunately the family moved from the city at the end of three months' observation, so that the final success cannot be stated.

It is felt that this report represents evidence of the psychic factors believed to be causal in enuresis, and particularly of the influence of these on cessation of the difficulty. To assume the tonsillectomy as provocative of results in the one instance requires a stretch of the imagination, although it is possible. But it could in no way explain the cessation in the sisters. Is it a phenomenon analogous, in a small way, to those of epidemics of hysteria, and to the many reported cures at places surrounded by a strong atmosphere of suggestion? In my opinion, this seems the probable explanation.

CONCLUSIONS

As one looks back over the results of this study, certain conclusions and impressions stand out. Some are clearly outlined and definite; some are tentative and suggestive; some are thoroughly negative. An attempt is made to subdivide the conclusions under these headings.

CONCLUSIONS ON THE CONTROL OR NORMAL GROUP

Among children of intelligent and educated parents the following data were obtained. This is considered suitable for standards and is so accepted: age of dentition, 8 months; age of talking, 14 months; age of walking, 13 months. Bowel control is obtained at an average age of 14 months; diurnal bladder control is secured at an average age of 17 months; nocturnal bladder control is secured at an average age of 23 months, with an average duration of a training period of six months.

The fact that about one half of almost all children used as controls sleep through the night invalidates the contention that the infantile bladder is too small to hold the night's secretion of urine. Temporary relapses through illness or other causes are not unusual, nor are they to be considered as serious.

The restriction of fluid is of little fundamental value. Seasonal variations are normal. Definite conditioning factors are of undoubted value in a large minority of cases; they may occasionally work negatively.

CONCLUSIONS OF MARKED DEFINITENESS AND SIGNIFICANCE

1. Emotional factors constitute by far the largest group of elements in the causation or, at least, the continuance of enuresis. Most contributory factors exert results on this basis.

2. Physical factors, while of undoubted significance in a limited number of cases, probably exert their greatest influence indirectly through suggestion and erroneous assumptions by parents and others as to being causative. To declare them of no importance in themselves is, in the majority of instances, impossible.

3. Habit training as reflected in attitudes and methods is one of the most important things to be considered as responsible for persistent enuresis.

4. Previous illnesses are factors of real importance in a large number of cases. This is mainly through relaxation of habit training rather than as a direct result of the illness.

5. Infantile traits appeared to be of high incidence among enuretic children. The bases of psychic infantilism are discussed. Temperamental children likewise constitute a large proportion in this group.

6. Timidity and sensitiveness characterize an unusually large percentage.

7. Nailbiting occurs in a high proportion of enuretic children, and appears to be an outlet for emotional energy arising from maladjustments from enuresis.

8. Feelings of inferiority are extremely common in such children. It is not believed that they are commonly causal, but that, having developed, they lead to the continuance of enuresis.

9. The intelligence of enuretic children is, on the whole, above the average, if one excludes a small group of intellectual defectives in which all training is difficult. More than one fourth of all enuretic children studied had an average intelligence quotient above 110, placing them in the superior group. An explanation of this is attempted.

10. Parental maladjustments occur with extreme frequency as producers of emotional upsets in children, obtaining in two thirds of all the children studied. Religious differences are one such source of trouble.

11. Parental attitudes, particularly those of "failure" and "severity," exert deleterious effects on measures for the control of enuresis.

12. Relationships between enuretic children and siblings are clearly etiologic to some extent in no small number of instances. Jealousy is perhaps the most common observation in this connection.

13. The conditioned reflex can account for many cases otherwise inexplicable.

14. About four fifths of all enuretic children coming to clinics for study manifest the strictly nocturnal type of enuresis. Eleven per cent present the combined day and night type, with only 3 per cent presenting the purely diurnal. Seven per cent of cases are complicated with soiling.

15. The frequency of enuresis among all cases studied averaged about five times weekly.

16. In more than 80 per cent of all cases the onset was from infancy, representing persistence of a once "normal" habit. In almost 20 per cent the onset was at some time following complete control of the bladder. It occurs as late as 12 years of age.

17. One fourth of all patients studied were considered cured and three fifths as either cured or definitely improved. Criteria of these terms are discussed.

18. Enuretic children show remarkable results in response to properly supervised hospitalization.

19. Enuresis is a severe problem among institutions. This phase is discussed with citations from several typical institutions.

TENTATIVE OR SUGGESTIVE CONCLUSIONS

1. Illegitimacy may exert an influence as a cause of inferiority feelings and hence of psycho-emotional unrest.

2. The duration of breast feeding may be of some significance, particularly as an index, or accessory cause, of already forming infantile traits.

3. Stealing and truancy probably have some relationship to enuresis in that they perpetuate affective disturbance.

4. Foster-homes and institutions are probably indirect contributing sources in a small number of cases.

NEGATIVE CONCLUSIONS

1. Neither race nor color are factors of appreciable importance.

2. The duration of gestation and character of birth cannot be considered as important factors, except in individual instances.

3. The time of development of certain fundamental processes, such as dentition, walking and talking, affords no significant data.

4. Height-weight ratios are not appreciably different between enuretic children and children used as controls.

5. Circumcision is not believed to be an important matter.

6. Left-handedness cannot be considered of importance in more than a very few cases.

7. Masturbation and enuresis do not appear to be substitutive equivalents, except in a few instances.

8. Tantrums are so universal in small children as to be considered normal. Their marked persistence beyond the age of average control of the bladder is indicative of infantilism, and is often associated with enuresis.

9. Thumbsucking cannot be considered as having a direct relationship to enuresis.

10. Aggressiveness and gregariousness are not traits of more than average development in enuretic children.

11. Depth of sleep is an observation so inconstant as to warrant no conclusions of its being causative.

12. Step-parent relationships do not seem to account for enuresis in many children.

13. The economic status cannot be considered of major importance. Its possibilities are discussed.

BIBLIOGRAPHY

1. Janet, J.: Les troubles psychopathiques de la miction, Thèse de Paris, 1890.

2. Langley and Anderson: J. Physiol. **19**:71, 1896.

3. Stewart, C. S.: On the Course of Impulses to and from the Cat's Bladder, Am. J. Physiol. **2**:182, 1898-1899.

4. Von Pfister, H.: Die Enuresis nocturna und aehnliche Storungen, Monatschr. f. Psychiat. u. Neurol. **15**:113, 1904.

5. Elliott, T. R.: Innervation of Bladder and Urethra, J. Physiol. **35**:367, 1907.

6. Fuchs, Alfred: Ueber den klinischen Nachweis kongenitaler Defektbildungen in den unteren Rückenmarkabschnitten (Myelodysplasie), Wien. med. Wchnschr. **59**:2142, 1909.

7. Hertoghe: Nouvelles recherches sur les insuffisances thyroidiennes; l'incontinence d'urine nocturne chez les enfants, et les adolescents, Bull. Acad. roy. de méd. de Belgique, 1909, vol. 24, no. 4.

8. Mattauschek: Ueber Enuresis, Wien. med. Wchnschr., 1909, vol. 59, no. 37.

9. Williams: Adenoids, Nocturnal Incontinence, and the Thyroid Gland, Lancet **1**:1245, 1909.

10. Herman, Charles: Treatment of Enuresis by Reeducation, Arch. Pediat. **27**:600, 1910.

11. Trommer, E.: Ueber motorische Schlafstörungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **4**:228, 1910.

12. Burnet, J.: Enuresis with Special Reference to Its Causation and Treatment, Internat. Clin. **21**:31, 1911.

13. Ewald and Heffler: Handbuch der allgemeinen und speziellen Arzneiverordnungslehre, Berlin, 1911.

14. Firth, A.: Enuresis and Thyroid Extract, Lancet **2**:1619, 1911.

15. Fleischner, E. C.: Some Points on the Etiology and Treatment of Enuresis, California State J. Med. **9**:67, 1911.

16. Klotz, M.: Therapeutisches zur Behandlung der Enuresis, der Incontinentia alvi und der Pyelitis, Berl. klin. Wchnschr. **48**:801, 1911.

17. Peritz, G.: Enuresis nocturna and Spina bifida occulta (Myelodysplasie), Deutsche med. Wchnschr. **37**:1256, 1911.

18. Radcliffe, A. A.: Takadiastase in Nocturnal Enuresis, Pediatrics **23**:617, 1911.

19. West, quoted by Fritsche: Zur Frage der Incontinentiae Urinae, Inaug.-Diss., Freiburg, 1912.

20. Lopez, Joseph: Enuresis and Cheiromania, Am. J. Dermat. & Genito-Urin. Dis. **16**:130, 1912.

21. Ruhräh: Treatment of Nocturnal Enuresis in Children, Am. J. M. Sc. **143**:185, 1912.

22. Mello-Leitao: Treatment of Nocturnal Enuresis in Children, Brit. J. Dis. Child. **9**:454, 1912.

23. Saenger, A.: Ueber Myelodysplasie und Enuresis nocturna, Deutsche Ztschr. f. Nervenh. **47-48**:694, 1912.

24. Shore, T. H. G.: Some Cases of Nocturnal Enuresis, St. Barth. Hosp. J. **20**:47, 1912.

25. Simpson, J. W.: Incontinence of Urine in Children, Edinburgh M. J. **10**:49, 1912.

26. Kaufmann, R., and Donath, H.: Ueber inverse Atropinwirkung, Wien. klin. Wchnschr. **26**:1193, 1912.

27. Robson, W. M.: Nocturnal Enuresis, Proc. Roy. Soc. Med. (Sect. Dis. Child.), 1912, vol. 6.

28. Van der Bogert, F.: Enuresis and Chronic Digestive Disturbances, Arch. Pediat. **30**:547, 1912.

29. Alexeieff, A.: Zur Diagnose duer Enuresis nocturna, Ztschr. f. Urol. **8**:451, 1914.

30. Barrington: Quart. J. Exper. Physiol. **8**:33, 1914.

31. Freeman, W. T.: Epidural Injections, Brit. M. J. **1**:1237, 1914.

32. Hale, G. C.: Case of Persistent Enuresis, Canad. M. A. J. **4**:413, 1914.

33. Moore, N. W.: Enuresis in Children, Kentucky M. J. **12**:778, 1914.

34. Philippart: Treatment of Infantile Nocturnal Enuresis, Gaz. méd. de Paris **85**:133, 1914.

35. Scharnke: Enuresis and Spina Bifida Occulta, Arch. f. Psychiat. **53**:43, 1914.

36. Schwartz, A. B.: Study of 226 Cases of Enuresis, Boston M. & S. J. **171**: 631, 1914.

37. Bach: Ztschr. f. Geburtsh. u. diaetet. Therap. **19**:75, 1915.

38. Cecil, A. B.: The Mechanism of Urination, J. A. M. A. **65**:1436 (Oct. 23) 1915.

39. Newlin, Arthur: Management of Enuresis, Arch. Pediat. **32**:753, 1915.

40. Poulsson: Lehrbuch der Pharmakologie, Leipzig, 1915.

41. Schwarz, O.: Versuch einer Analyse der Miktionsanomalien nach Erkältungen, Wien. klin. Wchnschr. **28**:1057, 1915.

42. Stier, E.: Abgrenzung und Begriff des neuropathischen Kindes, Deutsche med. Wchnschr. **41**:794, 1915.

43. Armbruster: Der Praktische Arzt, 1916, p. 25.

44. Dunham, F. L.: Suggestion as a Therapeutic Measure in Nocturnal Enuresis, Am. J. Dis. Child. **12**:618 (Dec.) 1916.

45. Hamburger, F.: Ueber Schlafstörungen im Kindesalter, Monatschr. f. Kinderh. **13**:23, 1916.

46. Klasi, J.: Ueber die psychogenen Ursachen der essentiellen Enuresis nocturna infantum, Ztschr. f. d. ges. Neurol. u. Psychiat. **35**:371, 1916.

47. Mendeloff, M.: Treatment of Nocturnal Enuresis, W. Virginia M. J. **10**: 258, 1916.

48. Spiller, W. G.: Congenital and Acquired Enuresis from Spinal Lesion, Am. J. M. Sc. **151**:469, 1916.

49. Noguès, P.: Symptomes objectifs de l'incontinence, dite essentielle, J. d'urol. **7**:39, 1917.

50. Slingerland, W. H.: Pamphlet issued from Russell Sage Foundation, 1917.

51. Adler, A.: Ueber den Druckin der Harnblase, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **30**:487, 1918.

52. Cameron, H. C.: Enuresis and Other Common Disorders of Conduct in Childhood, Practitioner **100**:112, 1918.

53. Emerson, W. R. P.: The Treatment of Enuresis Without Drugs, Am. J. Dis. Child. **15**:339 (May) 1918.

54. Grover, J. L.: The Etiology and Treatment of Enuresis, J. A. M. A. **71**:626 (Aug. 24) 1918.

55. Weitz, W., and Gotz, O.: Ueber die Pathogenese der Enuresis, Med. Klin. **14**:729, 1918.

56. Hernaman-Johnson: Practitioner **102**:239, 1919.

57. Pisek, G. R.: Common Disorders of Childhood, M. Clin. North America **3**:350, 1919.

58. Provinciali, U.: Essential Enuresis in Children, Pediatria **27**:567, 1919; abstr., J. A. M. A. **73**:1317 (Oct. 25) 1919.

59. Weitz, W.: Ueber die Behandlung der Enuresis, Med. Klin. **15**:761, 1919.

60. Aguilar, F. G.: Essential Incontinence of Urine, Siglo méd. **66**:1116, 1920; abstr., J. A. M. A. **74**:988 (April 3) 1920.

61. Borrino, A.: Riv. di psicol. applic. a pedagog., 1920, p. 189; abstr., Zentralbl. f. Kinderh., 1920, p. 9; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

62. Goppert and Langstein: Prophylaxie und Therapie der Kinderkrankheiten, Berlin, Julius Springer, 1920, p. 375.

63. Hamburger, R.: Therapeutische Erfahrungen mit der Quecksilberquarzlampe bei Kindern, Deutsche med. Wchnschr. **46**:147, 1920.

64. Von Kováts, F.: Aetiologie und Behandlung der Enuresis; abstr., Zentralbl. f. Kinderh., 1920, p. 9; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

65. Leopold, J. S.: Spina Bifida Occulta in a Child with Incontinence of Urine and Feces, J. A. M. A. **74**:439 (Feb. 14) 1920.

66. Pese, A.: Beiträge zur Pathogenese und Therapie der Enuresis, Jahrb. f. kinderh. **91**:357, 1920.

67. Pototzky, C.: Zur Behandlung der Enuresis nocturna, Deutsche med. Wchnschr. **46**:180, 1920.

68. Satzeff, Helene: Beiträge zur Enuresis infantum, Ztschr. f. d. ges. Neurol. u. Psychiat. **90**:1, 1920.

69. Schlomer, J.: Bettnassen und Erholungfürsorge, Ztschr. f. Selingesundheit. **33**:271, 1920.

70. Schwarz, O.: Untersuchungen ueber die Physiologie und Pathologie der Blasenfunction, Wien. Arch. f. inn. Med. **1**:455, 1920.

71. Barrington, F. J. F.: Brain **44**:23, 1921.

72. Bierens de Haan, P.: Treatment of Enuresis, Nederl. tijdschr. v. geneesk. **3**:1666, 1921; abstr., J. A. M. A. **77**:2154 (Dec. 31) 1921.

73. Bossert-Rollett, L.: Enuresis and Circulatory Disturbances, Deutsche med. Wchnschr. **47**:471, 1921.

74. Carrau, A.: Enuresis and Myelodysplasia, Rev. méd. d. Uruguay **24**:433, 1921; abstr., J. A. M. A. **78**:549 (Feb. 18) 1922.

75. Chetwood: Practice of Neurology, New York, William Wood & Company, 1922.

76. Carter, W.: Enuresis, Arch. Pediat. **38**:385, 1921.

77. DeAngelis: Pediatria, February, 1921; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

78. Fluehl, L.: Neues zur Lehre der Enuresis nocturna, Therap. d. Gegenw. **62**:257, 1921.

79. Fulton, G.: Nocturnal Enuresis, Kentucky M. J. **19**:736, 1921.

80. Gottfried, S.: Cause and Treatment of Nocturnal Enuresis, Ztschr. f. ges. Chir. **7**:160, 1921; abstr., J. A. M. A. **77**:979 (Sept. 17) 1921.

81. Hawks, C. C.: Southwest J. M. & S. **29**:53, 1921.

82. Hernaman-Johnson, F.: Treatment of Urinary Incontinence by Electrical Methods, Lancet **1**:1295, 1921.

83. Krafft, J. C.: Enuresis, Illinois M. J. **39**:50, 1921.

84. Lippmann, A.: Zur Entstehung und Behandlung der Enuresis, Deutsche med. Wchnschr. **47**:777, 1921.

85. Ortega, D.: Abstr., Zentralbl. f. Kinderh., 1921, p. 12; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

86. Pestalozzi, H.: Das Bettnaessen bei Kindern und Erwachsenen, Schweiz. med. Wchnschr. **5**:704, 1921.

87. Schmalfuss, G.: Aus der Praxis zur Behandlung der Enuresis nocturna, Deutsche med. Wchnschr. **47**:988, 1921.

88. Sundell, C. E.: Incontinence of Urine in Childhood, Practitioner **106**:293, 1921.

89. Abraham, K.: Ausdrucksformen des weibliche Kastrationskomplexes, Internat. Ztschr. f. Psychoanal., 1922, p. 434; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

90. Carrière, G.: Ueber die Mitteilung von Zuber ueber die Behandlung des unfreiwilligen Urinabganges durch Saeurung des Urins, Bull. Soc. de pédiat. de Paris, 1922, p. 220; abstr., Zentralbl. f. Kinderh., 1922, p. 14; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

91. Goldstein, F.: Zur Behandlung der Enuresis nocturna in Anstalten, Fortschr. d. Med. **40**:27, 1922.

92. Herbert, S.: The Psychogenic Root of Enuresis, Psychoanalyt. Rev. **9**:365, 1922.

93. Holmdahl, D. E.: Die Myelodysplasielehre, Monatschr. f. Kinderh. **25**:1, 1922.

94. Jacobs, F. B.: Diagnosis and Treatment of Nocturnal and Diurnal Enuresis, Pennsylvania M. J. **25**:867, 1922.

95. Klika, M.: Die Nervenkomplikationen der Phimose, abstr., Zentralbl. f. d. ges. Neurol. u. Psychiat., 1922, p. 31; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

96. Karger, P.: Die Hypokolasie, Jahrb. f. Kinderh. **98**:22, 1922.

97. Langer, H.: Enuresis und Tuberkulose, Ztschr. f. Kinderh. **33**:108, 1922.

98. Morichau-Beauchant, R.: False Incontinence in Children, Paris méd. **12**: 83, 1922.

99. Noeggerath: Jahrb. f. Kinderh. **100**:101, 1922.

100. Parahia, G.: Rev. espan. de ured., 1922, p. 27; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

101. Plato: Wearing of Urinal in Combating Enuresis, München. med. Wchnschr. **69**:438, 1922; abstr., J. A. M. A. **78**:1937 (June 17) 1922.

102. Pototsky, C.: Die Kampfertherapie der Enuresis, Deutsche med. Wchnschr. **48**:730, 1922.

103. Sironi and Saldattini: Riv. di clin. pediat., 1922, p. 309; abstr., Zentralbl. f. Kinderh., 1922, p. 14; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

104. Stekel, W.: Psychosexueller Infantilismus, Berlin, Urban & Schwarzenberg, 1921.

105. Thompson, A. R.: Some Cases of Incontinence of Urine, Brit. J. Dis. Child. **19**:30, 1922.

106. Zappert, J.: Die Behandlung der Enuresis, Klin. Wchnschr. **1**:37, 1922.

107. Amberg, S.: Some Aspects of Enuresis in Children, M. Clin. North America **7**:151, 1923.

108. Anderson, J. H.: Case of Nocturnal Enuresis Presumably Due to Defective Cerebral Development, M. J. Australia **1**:68, 1923.

109. Beadon, M.: Enuresis Treated by Electricity, Lancet **1**:283, 1923.

110. Benzing, R.: Erfahrungen ueber Enuresis und Enuresis-Behandlung, Ztschr. f. ärztl. Fortbild., 1923, p. 541; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

111. Behm, K.: Das Bettnaesserleiden; seine Behandlung und Bekaempfung, Ztschr. f. Gesundheit. u. Schulgesundheit. **36**:111, 1923.

112. Von Bucken, L.: Behandlung der Enuresis Nocturna mit Thermopenetration, Deutsche med. Wchnschr. **49**:586, 1923.

113. Courtin, W.: Die Beziehungen der Enuresis nocturna zum Schaffe, Arch. f. Kinderh. **73**:40, 1923; abstr., J. A. M. A. **81**:1866 (Sept. 8) 1923.

114. Cozzolino, O.: Enuresis and Deformity of Lower Spine, Pediatria **31**: 105, 1923; abstr., J. A. M. A. **80**:1418 (May 12) 1923.

115. De Angelis, F.: Camphor in Treatment of Enuresis, Pediatria **31**:761, 1923.

116. Fischer, F.: Aus der Praxis zur Bekaempfung der rein Enuresis nocturna, Med. Klin. **19**:142, 1923.

117. Gillmeister: München. med. Wchnschr., 1923, vol. 70.

118. Karger, P.: Suggestive Behandlung und heilpaedagogischer Bedingungsreflex, Monatschr. f. Kinderh. **25**:306, 1923.

119. Von Kovács, F.: Die funktionellen miktionsstoerungen tuberkulosen Ursprungs, Ztschr. f. Tuberk. **39**:185, 1923.

120. Morgagni: Pediatria **31**:105 and 349, 1923; abstr., Zentralbl. f. Kinderh., 1923, p. 14; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

121. Mosse, K.: Die Hypnose in Kindersalter, Monatschr. f. Kinderh. **25**:486, 1923.

122. Ochsenius, K.: Zur Behandlung der Enuresis, München. med. Wchnschr. **70**:432, 1923.

123. Saxl, N. T., and Kurzweil, P. M.: Enuresis in Children, Arch. Pediat. **40**:159, 1923.

124. Schwarz, O.: Ueber die Verwendung des Kalsiums bei Funktionsstörungen der menschlichen Harnblase, Wien. med. Wchnschr. **73**:18, 1923.

125. Stromayer, W.: Die Psychopathologie des Kindesalters, ed. 2, Munich, J. F. Bergmann, 1923.

126. Thursfield, Hugh: Treatment of Enuresis, Lancet **2**:528, 1923.

127. Walker, K. M.: Essential Enuresis, Practitioner **110**:145, 1923.

128. Zappert, J.: Ueber Neurosen inn Kindesalter, Arch. f. Kinderh. **73**:108, 1923.

129. Amberg, S.: Relations Between Contraction of Bladder and Impulse for Urination in Enuresis, Ztschr. f. Kinderh. **38**:146, 1924.

130. Amberg, Samuel: Certain Aspects of Enuresis, J. A. M. A. **83**:1300 (Oct. 25) 1924.

131. Arnesen, A. J. A.: Enuresis and Spina Bifida, Norsk mag. f. laegevidensk. **85**:*209*, 1924; abstr., J. A. M. A. **82**:1828 (May 31) 1924.

132. Bauer, A.: Krapperfolge bei Bettnaessen, Ztschr. f. Urol. **18**:452, 1924.

133. Boenheim, C.: Zur Enuresis-Frage, Therap. d. Gegenw., 1924, p. 253; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

134. Von Brunn: Zur Bettnaesserfrage, Ztschr. f. Schulgesundheit., 1924, p. 17; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

135. Chandler, A. B.: Enuresis, Canad. M. A. J. **14**:413, 1924.

136. Comby, J.: Traitement de l'incontinence d'urine chez les infants, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:*282*, 1924.

137. Delbet: Eingriffe gegen Enuresis; ihre Beziehung zur Spina bifida, abstr., Zentralbl. f. d. ges. Neurol. u. Psychiat., 1924, p. 38; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

138. Focher, L.: Versammete Deutscher Nervenärzte, Innsbruck, Zentralbl. f. d. ges. Neurol. u. Psychiat. **38**:*327*, 1924.

139. Fordyce, Thompson, et al.: Proc. Roy. Soc. Med. (Sect. Dis. Child.) **17**:*37*, 1924.

140. Gibbs, D. H.: Psychologic Factor in Enuresis, California & West. Med. **22**:*427*, 1924.

141. Gaett, T.: Handbuch der Kinderheilkunde, 1924, p. 519; cited by Zappert, Arch. f. Kinderh. **79**:144, 1926.

142. Karger, P.: Enuresis, Deutsche med. Wchnschr. **50**:639, 1924; abstr. J. A. M. A. **82**:2091 (June 21) 1924.

143. Janssen, P.: Incontinentiae Urinae bei dyspigischen Becken, Beitr. z. klin. Chir. **131**:586, 1924.

144. Kleeman, A.: Beiträge zur psychishen Behandlung der Enuresis, Ztschr. f. Kinderh. **38**:521, 1924.

145. Marcuse, M.: Das Bettnaessen als sexual neurotisches Symptom, Ztschr. f. Sexualwissensch. **11**:*239*, 1924.

146. Neurgerath and Erkstein, in Pfaundler and Schlossman: Handbuch der Kinderheilkunde, ed. 3, vol. 4, p. 49.

147. Pototzky, C.: Differentiation of Enuresis Types, Ztschr. f. Kinderh. **37**: 13, 1924; abstr., J. A. M. A. **82**:1088 (March 22) 1924.

148. Pugh, W.: Enuresis in Young Men, Am. J. Surg. **38**:34, 1924.

149. Salzeff, H.: Ztschr. f. d. ges. Neurol. u. Psychiat. **90**:1, 1924.

150. Thom, D.: Boston M. & S. J. **191**:145, 1924.

151. Thom, D.: U. S. Dept. Labor, Child. Bureau Bull. 135, 1924.

152. Viola, E.: Treatment of Enuresis, Riforma med. **40**:633, 1924; abstr. J. A. M. A. **83**:649 (Aug. 23) 1924.

153. Wile, I. S., and Orgel, S. Z.: Nervous Basis of Enuresis, Arch. Pediat. **41**:*232*, 1924.

154. Bonacorsi, L.: Pituitary Extract in Treatment of Enuresis, Pediatria **33**:936, 1925; abstr., J. A. M. A. **85**:1434 (Oct. 31) 1925.

155. Broza, J.: Ueber das naechtliche Bettnaessen, Arvose Hetilap, 1925, p. 69; abstr., Zentralbl. f. Kinderh., 1925, p. 18; cited by Zappert, Arch. f. Kinderh. **79**:44, 1926.

156. Von During: Vortrag Aerzte geschellsch., Frankfurter, München. med. Wchnschr. **72**:1053, 1925.

157. Freud, P.: Beitrag zur Therapie der Enuresis nocturna, Med. Klin. **21**: 1729, 1925.

158. Gegenbach, F. P.: Dietary Administration and Therapy, 1925.

159. Gram, C.: Present Status of Enuresis, Ugesk. f. laeger. **87**:739, 1925.

160. Heller, T.: Grundriss der Heilpaedogisch, ed. 3, Leipzig, Wilhelm Engelmann, 1925.

161. Von Kováts, F.: Ztschr. f. Tuberk. **42**:297, 1925.

162. Levy, S.: Blasendehnung bei Bettnaessen, Deutsche med. Wchnschr. **51**: 1201, 1925.

163. Moss, S. A.: Enuresis, M. J. & Rec. **121**:22, 1925.

164. Mueller, P.: Die Beeinflussung der Enuresis durch Tuberkulinjektionen, Ztschr. f. Tuberk. **42**:294, 1925.

165. Noeggerath: München. med. Wchnschr. **72**:1342, 1925.

166. Ochsenius, K.: Zur Behandlung der Enuresis, München. med. Wchnschr. **72**:1342, 1925.

167. Schwarz, O.: Psychogenese und Psychotherapie korperliche Symptome, Berlin, Julius Springer, 1925, p. 273.

168. Serantes, A., and Montes, L.: Enuresis in Children, Rev. Soc. argent. de urol. **1**:139, 1925.

169. Sicard, J. A.: Enuresis, Ann. de méd. **17**:470, 1925; abstr., J. A. M. A. **85**:220 (July 18) 1925.

170. Weissenberg, W.: Ueber das Bettnassen und die Rolle der Traume in seinem Bilde, Ztschr. f. Kinderh. **40**:343, 1925.

171. Benjamin, J., and Lauer, J.: Preliminary Report on a Clinical Study of Enuresis, J. Deling. **10**:389, 1926.

172. Bernn, M.: Ugesk. f. laeger. **88**:784, 1926.

173. Birk, W.: Jahrb. f. Kinderh. **110**:226, 1926.

174. Dennig, H.: Die Innervation der Harnblase, Berlin, Julius Springer, 1926.

175. Deutsch, I.: Peculiar Changes in Posterior Urethra in Enuresis, Ztschr. f. Urol. **20**:1, 1926; abstr., J. A. M. A. **86**:1175 (April 10) 1926.

176. Erickson, W. J.: Enuresis, M. J. & Rec. **124**:493, 1926.

177. Homburger, A.: Psychopathologie des Kindesalters, Berlin, Julius Springer, 1926, p. 557.

178. Ernest, J. H.: Good Housekeeping **84**:133, 1926.

179. Sarath, A.: Eine kausale Therapie der Enuresis nocturna, Klin. Wchnschr. **5**:1446, 1926.

180. Bistschel, H.: Ueber Enuresis in Kindesalter, Ztschr. f. Urol. **20**:664, 1926.

181. Paterson, D.: Frequency of Micturition in Infancy and Childhood, Practitioner **116**:418, 1926.

182. Woolley, Helen: Enuresis as a Psychological Problem, Ment. Hyg. **10**:35, 1926.

183. Wylder, M. K.: Etiology and Treatment of Enuresis, M. J. & Rec. **123**: 358, 1926.

184. Zappert, J.: Ein Referat ueber die Arbeiten der letztenfünf Jahre, Arch. f. Kinderh. **79**:44, 1926.

185. Blatz, W. E.: Second Conference on Child Development, Washington, May, 1927, Pub. by Div. of Anthropology and Psychology of Committee on Child Development.

186. Boenheim, C.: Ztschr. f. Kinderh. **43**:211, 1927.

187. Cameron, H. C.: Guys Hosp. Rep. **77**:482, 1927.

188. Cimbal, W.: Die Neurosen des Kindesalters, Berlin, Urban & Schwarzenberg, 1927, p. 43.

189. Friedell, A.: Reversal of the Normal Concentration of Urine in Children Having Enuresis, Am. J. Dis. Child. **33**:717 (May) 1927.

190. Muhl, A. M.: Emotional Maladjustment During Pregnancy with Possible Relationship to Enuresis in the Child, Psychoanalyt. Rev. **14**:326, 1927.

191. Muldawer, F. J.: Arch. Pediat. **44**:429, 1927.

192. Partridge, M. N.: Study of Nocturnal Enuresis in Boys, J. Delinq. **11**: 296 (Dec.) 1927.

193. Schroeder, P. L.: Enuresis in Adolescent Boys, Arch. Neurol. & Psychiat. **18**:1053 (Dec.) 1927.

194. Stutzen, J. J.: Med. Klin. **23**:1361, 1927.

195. U. S. Children's Bureau, Pub. no. 143, revised, 1927, p. 33.

196. West, J. W.: Notes on an Investigation into the Relation Between Enuresis and Spina Bifida Occulta, J. Roy. Army M. Corps **48**:38, 1927.

197. Calvin, J. K.: Enuresis, J. A. M. A. **90**:820 (March 17) 1928.

198. Mitchell, J. M.: Atlantic M. J. **31**:469 (April) 1928.

199. Barrington, F. J. F.: Central Nervous Control of Micturition, Brain **51**:209, 1928.

Pediatric Biographies

GERONIMO SORIANO

1575-?

JOHN RUHRÄH, M.D.
BALTIMORE

If there are many books on diseases of children in Spanish prior to 1800, they are difficult to find. Luis Lobera of Avila wrote one, Francisco Perez another and Damian Carbon, of Mallorca, gave quite an extended account of the care of children and of their diseases in his "Libro del arte de las comadres." All of these are rare. A trip to Spain would doubtless lead to the discovery of others.

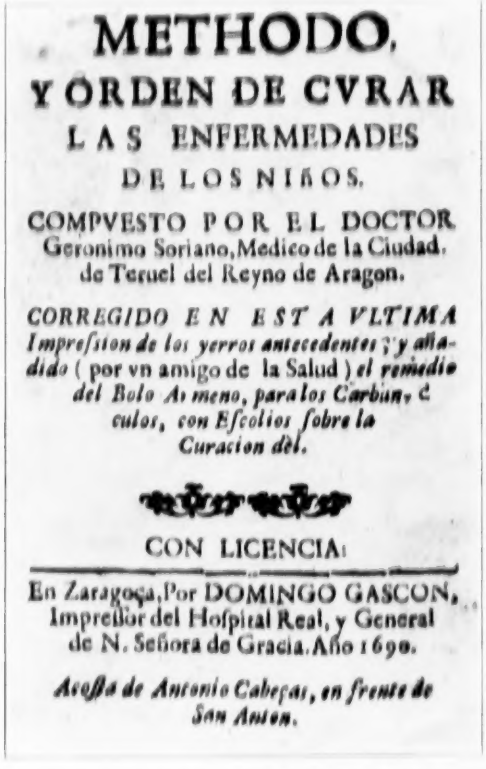
Another book of great interest for various reasons is the "Method and Order of Curing the Diseases of Children," which the title page states was "composed by the Doctor Geronimo Soriano, Physician of the City of Teruel of the Kingdom of Aragon." It was printed, "con licencia," in Zaragosa by Domingo Gascon, Printer of the Royal Hospital and General of Our Lady of Grace in the year 1690, alongside of Antonio Cabeças, opposite San Anton. All of these good worthies have passed away, but this little book of Soriano's still survives to tell us of them.

Nothing is known of Soriano and "La historia de la medecina española" of Chinchilla states only that he was a physician in Teruel. He wrote another book entitled "Experimentos medicos," which was published in 1599. There had evidently been a previous edition of the little book on children, perhaps more than one, for the title page also states that it "was corrected in this last impression of former errors and added (by a friend of health) the remedy of Bolo Armeno for Carbuncles, with notes on the cure of (the same)."

In many of the older books one finds that they are printed "by privilege" or "by license" and so on, these phrases being the hallmark of the censor representing church or state through whose hands the book had passed. Soriano's book is interesting in that it passed the censor both of the church and of the king and has these permits printed in full in place of the mere words "con licencia."

While today one sits supinely and watches rights and privileges taken away one by one, and witnesses the passage of a censorship bill without a protest, this book is an eloquent evidence of what has happened in the

past and of what will happen again. Suppose every article on the diseases of children had to be passed on by the representative of some bishop, say one from Tennessee, and by the city, state or national government, or all four. This state of affairs is not so far away as the casual reader might imagine, and here is one of the reasons for the study of medical history and biography somewhat marred by the Cassandra-like characteristics of medical historians when it comes to matters of state or, as it should be put, politics.



METHODO,
Y ORDEN DE CVRAR
LAS ENFERMEDADES
DE LOS NIÑOS.

COMPVESTO POR EL DOCTOR
Geronimo Soriano, Medico de la Ciudad
de Teruel del Reyno de Aragon.

CORREGIDO EN ESTA VLTIMA Impreſsion de los yerros antecedentes; y añadido (por vn amigo de la Salud) *el remedio del Bolo Armeno, para los Carbunculos, con Eſcolios ſobre la Curacion dèl.*

CON LICENCIA:

En Zaragoça, Por DOMINGO GASCON, Impreſſor del Hoſpital Real, y General de N. Señora de Gracia. Año 1690.

A coſta de Antonio Cabeças, en frente de San Anton.

Fig. 1.—Title page of Soriano's book.

The license from the church reads as follows:

The Licentiate Mateo de Causeco, in the spiritual and temporal, vicar General of the city and archbishopric of Zaragossa, by the most Illustrious and most Reverend Senor D. Alonzo Gregonio, by the Grace of God, and of the Holy Apostolic Seat, Archbishop of Zaragossa, of the Council of His Majesty, etc. We give licence to publish this book, entitled Methodo de curar las enfermedades de los niños, composed by Doctor Jeronie Soriano, Doctor in all of this archbishopric. We certify that there is nothing in this work opposed to our holy Catholic Faith and good morals. Given in Zaragossa the 16th of June, 1688.

The Licentiate Mateo de Canseco. By order of the said Vicar General, Basulio Gil Notary.

And there follows, taking second place, the permission of the deputy of the king:

We Don Philip by the Grace of God King of Castille, of Aragon, of Leon, of Jerusalem, etc.

We Don Bellian de la Cueva, Duke of Alburquerque, Marquis of Cuellar, Count of Ledesma and Guelma, Deputy and Captain General for his Majesty in

EL Licenciado Mateo de Canſeco, en lo Eſpiritual y Temporal, Vicario General de la Ciudad y Arçobiſpado de Zaragoça, por el Iluſtriſsimo, y Reverendiſsimo Señor D. Alonſo Gregorio, por la gracia de Dios, y de la Santa Sede Apoſtolica, Arçobiſpo de Zaragoça, del Conſejo de ſu Mageſtad, &c. Damos licencia para que ſe pueda imprimir eſte libro intitulado, Methodo de curar las enfermedades de los niños, compueſto por el Doctor Geronimo Soriano, Medico en todo eſte Arçobiſpado. Por quanto nos conſta no ay en el coſa que contravenga à nueſtra ſanta Fè Catolica y buenas coſtumbres. Dada en Zarogoça à diez y ſeis de Iunio, del año de mil y ſeiſcientos.

El Licenciado Mateo de Canſeco.

Por mandado de dicho Vicario Genral,
Braulio Gil Notario.

A ſ Nos

Fig. 2.—"Privelege" of the Church, granting permission to publish Soriano's book.

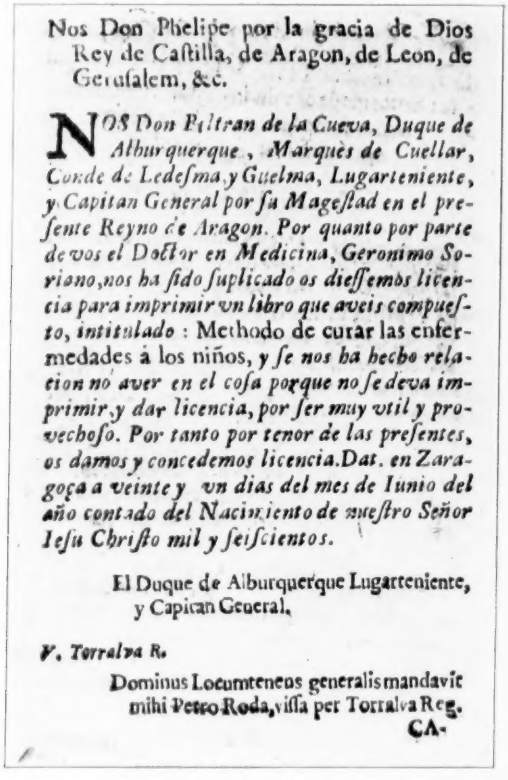
the present Kingdom of Aragon. Whereas the Doctor of Medicine Geronimo Soriano has begged us that we give him permission to print a book which he has composed, entitled "Method of Curing the Diseases of Children" and has made a report to us that there is no reason why it should not be printed or have license because it is very useful and beneficial, wherefore by contents of these presents we give and concede the License.

Given in Zaragossa the 21st of June of the year counted from the Birth of Our Lord Jesus Christ, 1680.

The Duke of Alburquerque Deputy and Captain General.

Soriano evidently owned or had access to the work of Eucharius Rhodion, or Rösslin, in one of the many editions containing a work on diseases of children which had its origins in Metlinger's book but which many printings and many unknown hands had changed extensively. He mentions him on the first page. His method was to state what Rösslin had to say, and then follow it with his own Scholia or notes.

There are thirty-nine such chapters starting with a short general chapter on disease in children and followed, perhaps through its impor-



Nos Don Phelipe por la gracia de Dios Rey de Caſtilla, de Aragon, de Leon, de Gerusalem, &c.

NOS Don Feltran de la Cueva, Duque de Alburquerque, Marquès de Cuellar, Conde de Ledesma, y Guelma, Lugarteniente, y Capitan General por su Mageſtad en el preſente Reyno de Aragon. Por quanto por parte de vos el Doctor en Medicina, Geronimo Soriano, nos ha ſido ſuplicado os dieſſemos licencia para imprimir vn libro que aveis compueſto, intitulado: Methodo de curar las enfermedades à los niños, y ſe nos ha hecho relacion no aver en el coſa porque no ſe deva imprimir, y dar licencia, por ſer muy vtil y prouechoſo. Por tanto por tenor de las preſentes, os damos y concedemos licencia. Dat. en Zaragoça a veinte y vn dias del mes de Iunio del año contado del Nacimiento de nueſtro Señor Ieſu Chriſto mil y ſeiſcientos.

El Duque de Alburquerque Lugarteniente, y Capitan General.

V. Torralva R.

Dominus Locumtenens generalis mandavit mihi Petro Roda, viſſa per Torralva Reg. CA-

Fig. 3.—"Privelege" of the State, granting permission to publish Soriano's book.

tance in a country with a burning hot summer, by an article "De la curacion de las camaras" or the cure of diarrhea, which is followed by "De quando no pueden hazer camara," when one cannot pass a stool, which is followed by convulsions. There are chapters on coryza and cough, on the cure of difficult breathing which the Greeks call dyspnea, and so on through the usual list, ending up with the equivalent of "If any one has been helped let him give thanks to God," a somewhat equivocal statement to say the least.

The therapy is that of the period touched by the localisms of Aragon, the infusions of various plants, rose leaves, saffron, and the like, of mixtures of various fluors, of decorticated lentils and other grains, of various oils and tablets made with tragacanth, of egg mixtures, of litharge and other things too numerous to mention.

Soriano was either a moralist or one who wrote at times with his tongue in his cheek for he gives directions for waters to remove or alleviate smallpox scars and other blemishes of which he says in closing that chapter:

> I have desired to place here the method of making these waters so that honest women if they take husbands full of desire or libidinous, will so attract them that they will not go to other women but be content with the presence of the wife. Do not understand that it is my intention to give them occasion to sell themselves better or to abandon themselves, because my only intention is that each one may serve God and her husband as a Christian.

As will be seen from the one excerpt, the ammoniacal diaper and chafing is no new problem. It goes back in literature to the Arabians and doubtless much further. On this question Soriano has the following chapter:

> Of Excoriation, Chafing and Sores Caused by the Urine.
>
> For chafing, sores or excoriation caused by the mordacity and acrimony of the urine in young children take powdered myrtle and strew it over the excoriation, chafing or sores.
>
> Another remedy.
>
> Take hedge mustard (called *rinchaon*), colored roses, sweet cypress and tragacanth, of each a dram, mix them all and place over the part excoriated or use a powder of some of the said things.
>
> Another remedy.
>
> Take of oil of roses one ounce, of white incense a dram, and dissolve in them eight grains of caphura steeped in water of roses; make an ointment of all these and with it anoint the excoriated and chafed parts.
>
> Anointing with white or red ointment or with white lead is good in case of excoriation or chafing.

NOTES

This infirmity in children is persistent because of the many remedies advised by physicians, none are used. Also because there are few who fear it although there are many who refresh and clean it. Because there are cases where the nurses or mothers take care to keep the children clean but are so voracious and such gluttons and gobblers and all of them such good spinners (and not of cotton) that they do not hesitate to eat anything, even garlic, onions, salted things, fish and drink without measure and without a drop of water so that the milk they give the children is acid and mordant, so that the urine and feces of the babies are also acid and mordant, as it has to come out acid and mordant not only in the stools but the urine and so scalds, chafes and irritates the tender little thighs. This disease is so common and as I have said in spite of the advice of physicians, the women use other remedies, many of which the author gives here. In my children, it is seen very seldom, praise be to God, and when it sometimes

happens I only have them use over the sore place a little woodlouse dust (which in Aragon we call *quera*) of old wood and they are cured at once. Of the principalness of the virtues of woodlouse dust and of its effects and of which woods are the best we treat of in the chapter on malignant ulcers in our book entitled *Experimentos medicos*.

Some women use other remedies which they find good. Some use on the sore places earth (which others call earth of "*Pelayres*," Fuller's earth) either powdered by itself or mixed with oil of roses and it is good.

Others use barley flour mixed with lentil flour and this is successful.

All are good remedies taken from Avicenna; because according to that author myrtle contracts and hardens and thus is useful for cicatrizing, for burns, for chafing and excoriations, for pustules and other similar affections. Dried roses, according to Dioscoriedes, are admirable for this purpose, because they refresh, dry, strengthen and restore the skin and the thin and subtile pellicle. The sweet cypress dries without irritating, and thus according to Galen is useful for ulcers that are difficult to heal. Barley flour dries and refreshes and in some way cleans; that of lentils contracts much and binds without fever or chilling and thus the mixture of one flour with the other in equal parts used on the irritation, chafing or scalding is most useful because it cleans, dries and cures the excoriation and chafing without irritation or acrimony.

Some use over the excoriation powder of the roots of the purple *lilio* because it dries, cleans, softens, resalves, mitigates, opens and also purifies. But before using these remedies or applying them it is good to do what Aecio says, which is to first wash the parts with wine and afterwards use the powders.

With all the said advice take care that the nurse eat things which refresh and which stop the mordacity and acrimony of the milk which leave the body of the child in the urine and excrement and to make good milk, good meats, chicken and young chicken, squab, capon or veal and not salt meats, cheese, fish, olives nor peppered things.

The wine which they drink should be good and well watered and with all this it is needful to keep the baby clean so that neither the urine nor feces chafe or excoriate it. When infants suffer from chafing or soreness give them by mouth from time to time some spoonfuls of syrup of violets and of red roses mixed.

News and Comment

GENERAL

Dr. F. J. Poynton Awarded Sir Dawson Williams Memorial Prize.—Dr. Frederick J. Poynton, Senior Physician to the Hospital for Sick Children, London, has received the first award of the Sir Dawson Williams Memorial Prize, consisting of 50 guineas, for his work in behalf of children with rheumatism.

Philadelphia Closes Diphtheria Hospital.—Philadelphia has had such a reduction in the morbidity from diphtheria that it has been found no longer necessary to maintain a diphtheria hospital.

Virginia Provides Care for Crippled Children.—Virginia has instituted a new program of state care for crippled children. Children are to be treated in their homes with the cooperation of local physicians when possible. In severer cases the patients will be sent to hospitals.

"Bobby Jones Fund" Created for Children's Hospital Playground.—At the James Whitcomb Riley Hospital for Children, Indianapolis, there is a fund of approximately $1,000, known as the Bobby Jones Fund, which was raised at two exhibition golf games played by Jones in 1926. This will be expended on the playground of the hospital.

Dr. Amesse Appointed to Subsidiary Board of Medical Examiners.—In a recent issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN the fact that a pediatrician had not been appointed to the National Board of Medical Examiners was mentioned. In *"The Diplomat,"* Denver, part 3, it is stated that Dr. John W. Amesse has been made a member of the Subsidiary Board. It is hoped that this is an indication of enlightenment on the part of this most estimable organization.

Children's Convalescent Home Under Construction in Milwaukee.—Construction of a sixty bed convalescent home in connection with the Milwaukee Children's Hospital is being started. It is the gift of Mr. and Mrs. L. R. Smith and is to be furnished and equipped throughout by Mrs. A. Lester Slocum. The cost of the building with its grounds will be $250,000.

Milwaukee Hospital Auxiliary Given Profits from Polo Field.—The Seeger polo field, belonging to Dr. and Mrs. S. J. Seeger, has been opened to the public in the interest of the Milwaukee Children's Hospital Auxiliary and its Prevention of Burns Committee.

UNIVERSITY NEWS

The Children's Free Hospital of Louisville has become affiliated with the University of Louisville School of Medicine, the medical staff to be appointed by the Board of Directors on nomination by the University of Louisville Trustees. Dr. Philip F. Barbour is chief of staff.

Dr. William Palmer Lucas, for several years head of the Department of Pediatrics, University of California Medical School, was tendered a banquet and presented with a gold watch on his retirement at the end of the last academic year.

Graduate courses in pediatrics are to be given at the University of Michigan in October, November, December, February, March and April under the auspices of the Michigan State Medical Society.

The list of courses for students at Vienna from Sept. 1, 1930, to Oct. 31, 1931, includes:

A group course on pediatrics by Professor Hamburger and his assistants. This is a comprehensive course and comprises in all from thirty-one to thirty-six hours' work in two weeks.

There is another course by Prof. Leopold Moll, mostly on nutrition and respiratory conditions. This consists of twelve hours' work in two weeks.

There are monthly courses in pediatrics by various well known instructors, including Drs. Alois Bratusch-Marrain, Friedjung, Helmreich, Kornfeld, Lehndorff, Mautner, Neurath, Nobel, Orel, Priesel, Salzer, Wagner and Zappert.

SOCIETY NEWS

Sociedad Peruana de Pediatria.—There has been formed at Lima, Peru, the Sociedad Peruana de Pediatria with Prof. Enrique León Garcia as president and Dr. Z. A. Cardenas as secretary.

Sociedad de Pediatria de Bahia.—At Bahia, Brazil, there has been formed the Sociedad de Pediatria de Bahia, with Prof. Alfredo Magalhaes as honorary president, Prof. Martagao Gestira as president and Alvaro da Franca Rocha as secretary.

DEATHS

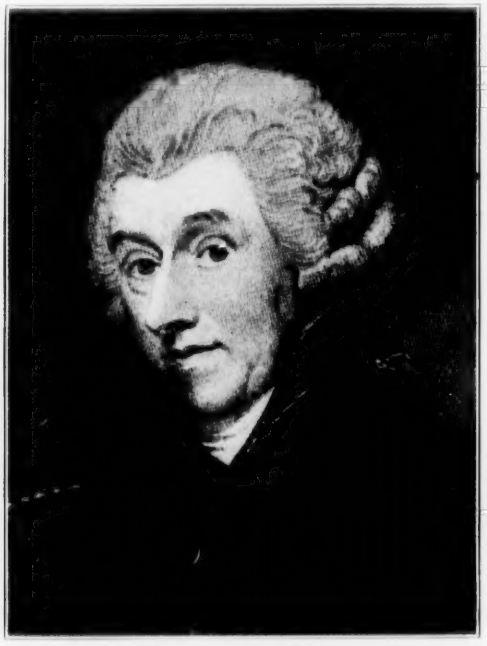
Dr. Adolphe D'Espine, the well known pediatrician whose sign is often quoted, died recently in Geneva.

Dr. Guida Tommaso died in Naples on September 1.

There recently died the well known Hungarian pediatrician, Dr. Felix von Szontagh.

CORRECTION

Through an error, a photograph of Benjamin Rush was published in the biography of William Heberden the Elder in the September issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN. Dr. Heberden's picture is reproduced here.



DR. HEBERDEN

Abstracts from Current Literature

Anatomy and Physiology

The Roentgenogram in Mastoid Disease. Henry K. Taylor, Am. J. Roentgenol. **19**:522 (June) 1928.

Mastoid roentgenography is an aid to otologic diagnosis, but should not overweigh the clinical observations. A roentgenogram of the mastoid should give the following information: anatomic data, variations in density, absence or presence of a destructive lesion and absence or presence of a productive lesion. A history of a previous acute otitic infection must be taken into consideration when estimating the significance of a localized area of destruction on a roentgenogram. Mastoiditis that shows only a mild involvement, as evidenced by decreased illumination and slight destructive changes, may clear up without operative intervention. A progression of destructive changes in an acute otitic infection indicates that the lesion is active. The finding of a sclerotic mastoid is in itself no indication for operation. The clinical observations should furnish the chief guide to procedure.

Stulik, Chicago.

Congenital Absence of Femur, Patella, Tarsal Scaphoid and Ischium Associated with Other Abnormalities: Case Report. A. R. Shands, Jr., Am. J. Roentgenol. **19**:531 (June) 1928.

A man, aged 24, presented the following congenital anomalies: complete absence of the right thigh; absence of the shaft of the right femur, with a small caput epiphysis remaining, and a fusion of the lower femoral epiphysis with the tibia; in the pelvis, a complete absence of the right ischium and the inferior ramus of the right pubis, an imperfect and small right ilium, an imperfect and small right side of the sacrum and an articulation between the right pubis and sacrum; a complete absence of the right patella; a complete absence of the right tarsal scaphoid; bony defects in the parietal bones, with an oxycephalic head, and nondescent of the testes. A partial review of the literature on the congenital bony anomalies involved is given.

Stulik, Chicago.

The Value of Shenton's Sign in the Roentgen Diagnosis of Congenital Luxation of the Hip in Early Childhood. A. Mezzari, Radiol. med. **15**:13 (Jan.) 1928.

The usual signs for demonstrating congenital luxation of the hip are hard to demonstrate in young infants; the author therefore calls attention to the value of Shenton's sign. Shenton found that in a hip that is well centered a prolongation of the upper border of the obturator foramen exactly joins a line passing through the lower margin of the neck of the femur, describing a segment of a circle which is called Shenton's cervico-obturator line. When the normal relation of the bones is disturbed, this line is interrupted. It has been called a positive Shenton sign when the line is interrupted by upward displacement of the proximal end of the femur and negative when the displacement is downward. But the author thinks that any interruption should be called a positive Shenton's sign and the word downward added if the displacement is in that direction. Downward displacement is rare and is usually due to trauma. In the cases of luxation of the hip in young infants treated by the author the sign was always positive. The roentgenogram must be taken with an absolutely frontal position of the pelvis. In coxa vara congenita, which may be confused with congenital luxation of the hip, the line is enlarged but not interrupted. It may be inter-

cupted in luxation of the hip from suppuration or tuberculosis, but the differentiation can be made in these cases by the history and course of the disease and by the fact that the roentgenogram shows signs of a destructive process.

[Am. J. Roentgenol.]

Roentgenologic Studies of the Heart in Children. H. Lehmkuhl, Jahrb. f. Kinderh. **128**:166 (Feb.) 1929.

Lehmkuhl presents average values for the diameter of the heart and the heart surfaces, which are fairly constant values for the ages given. With increasing age the values do not increase proportionately as would be expected. The investigations of the volume of the heart cannot as yet be considered complete.

A. F. Abt, Chicago.

The Physiology of the Water Economy in Infants. Oskar Bosch, Ztschr. f. Kinderh. **48**:413, 1929.

In twenty-six infants in the fourth and fifth month, after a grounding foreperiod, the activity of water excretion was followed under complete physiologic conditions of nutrition, clothing and external surroundings. There were great variations, not only in different children of the same age, but in the same child on different days. The ratio of the renal and extrarenal output of water, the four-hour balances, etc., are given as averages. The amount of water excreted varied in spite of regularity in feeding. Of the different meals from day to day, different amounts of fluid were retained. The retentions were smoothed out in the early morning hours, called the smoothing-out time, and thus the normal daily gains in weight were checked. Through the retentions and their smoothing out there arose variations in the interdiurnal weights; the weight of a 5 Kg. infant varied 143 Gm. on the average in the course of twenty-four hours. Attention is called to transient unexplained variations in the normal output which are followed by compensatory reactions. This peculiar variation and its compensation, which varied with the daily and nightly outputs, are the cause of the great spread of the amounts excreted; herein lies the explanation of the present chaos in the water economy of infants aged 1 and 2 months. All the figures given are valid only for the foreperiod and for all the experimental conditions observed by the investigators. They would like their average figures to be looked on as comparative values.

Emerson, Boston.

Roentgenologic Determinations of the Size of the Heart in Infants and Children. Ernst Voss, Ztschr. f. Kinderh. **48**:428, 1929.

For the judgment of the size of the heart by roentgenography, a great number of patients must be measured; this will give more reliable figures than the exclusive use of the heart chest quotient of Grondel. The transverse diameter and the length of the heart are safe measurements, whereas the breadth, the area and the volume are not. The size is more influenced by the length of the body and the weight, than by the age and the circumference of the chest. The transverse diameter changes faster in infancy than in later periods of life, as does the length of the heart. The close roentgenogram (65 cm.), according to Grondel, is valid up to the end of the fourth year. It is necessary to continue to use roentgenography in infants and children because it is more reliable than percussion, though it is costly and inconvenient.

Emerson, Boston.

The Calcium Content of Blood Serum in D-Hypervitaminosis. J. Warkany and A. Wasitzky, Ztschr. f. Kinderh. **48**:442, 1929.

In guinea-pigs and rabbits the phosphatemic curve is increased in from twenty-four to forty-eight hours after the use of irradiated ergosterol (50 mg.); but no

increase in the fasting value for calcium within the same time could not be established with certainty. The great increase in the value of phosphorus during the phosphatemic reaction did not result in any corresponding change in the value of calcium, so that the product Ca × P, which normally is about 50, might climb on the average to 127.2 and the quotient $\frac{Ca}{P}$, normally 1.95, might sink on the average to 0.98.

EMERSON, Boston.

Pathology, Bacteriology and Biochemistry

POLIOMYELITIS ANTISTREPTOCOCCUS SERUM. E. C. ROSENOW, J. A. M. A. **94**: 777 (March 15) 1930.

The streptococcus with peculiar neurotropic and immunologic properties has been cultivated from the throat, brain and cord, and for the first time in pure culture from the spinal fluid in cases of typical poliomyelitis. It has been demonstrated constantly in smears of the spinal fluid in twenty-three cases, and in each of twelve monkeys that had typical poliomyelitis following inoculation of the virus. The therapeutic action of the serum in the treatment of a new series seemed unmistakable. It is concluded that polio-antistreptococcic serum has curative power in poliomyelitis.

BOSAN, Salt Lake City.

STREPTOCOCCI FROM SCARLET FEVER, ERYSIPELAS AND SEPTIC SORE THROAT; EFFECT ON CHOCOLATE AGAR. RUTH TUNNICLIFF, J. A. M. A. **94**:1213 (April 19) 1930.

Hemolytic streptococci from typical cases of erysipelas produce a bright green on chocolate agar in one or two days. Those from scarlet fever cause either no change or occasionally a slight greening of the medium after several days' growth. Immunologically, hemolytic streptococci from septic sore throat do not belong to either the scarlet fever or the erysipelas group.

BOSAN, Salt Lake City.

THE PATHOGENESIS OF, AND PROPAGATION OF THE VIRUS IN, EXPERIMENTAL POLIOMYELITIS. R. W. FAIRBROTHER and E. WESTON HURST, J. Path. & Bact. **33**:17, 1930.

After intranasal and intracerebral inoculation in monkeys, poliomyelitis spreads histologically from above downward, the various levels of the cord becoming involved more or less simultaneously. Owing to the greater individual susceptibility of the anterior horn cells, and particularly those of the lumbar region, paralysis usually appears, and later becomes complete, first in the legs; the clinical signs are thus no guide to the path of entry or manner of spread and development of the disease. Spread of the infection to the brain stem and cord occurs by way of the axis cylinders and this appears to be the route usually taken to other parts of the central nervous system; meningeal spread is, however, possible and probably always plays some part in the local dissemination of the infection around the site of inoculation. Meningitis is therefore not the primary lesion of the disease, which begins as a primary degeneration of nerve cells accompanied by inflammation in the interstitial tissues. Virus is present in greatest amount in those regions in which nerve cell degeneration is particularly severe, that is to say in the spinal cord and brain stem; where nerve cell degeneration is slight, as in the cerebral cortex, in spite of the existence of numerous foci of inflammation, the virus is found inconstantly. The cerebral cortex is not a favorable site for survival of the virus which tends within a few days to disappear altogether from the site of inoculation. If the virus travels chiefly by way of the axis cylinders, its appearance in the cerebrospinal fluid would not be expected, nor, in fact, is it found there except on rare occasions.

AUTHORS' SUMMARY.

VISCOSITY OF THE BLOOD IN INFANTS AND CHILDREN. V. MIKULOWSKI and H. CHMIELEWSKA, Rev. franç. de pediat. **5**:706 (Dec.) 1929.

Blood viscosity, determined with the Hess apparatus, was studied in relation to blood pressure, hemoglobin, red and white cell counts, index of refraction and albumin content. In 100 normal children varying in age from 1 to 15 years, the viscosity was found to be between 4.5 and 5. In children with anemia it was lowered. Increase in viscosity coincident with normal or low blood pressure is fairly frequent. It is found in cardiovascular disturbances, leukemias, chronic respiratory diseases, such as tuberculosis, in the course of convalescence from acute infections, and in cases of asthenia related to disturbance of the vegetative nervous system.

LESLIE, Evanston, Ill.

THE ENZYME ACTIVITY OF THE PANCREAS IN THE INFANT. G. MACCIOTTA, Rev. franç. de pédiat. **6**:72, 1930.

Examination of the duodenal content in thirty-six infants shows that from 5 to 10 cc. of pancreatic juice enters the duodenum each quarter of an hour in the first week of extra-uterine life, from 8 to 15 cc. toward the end of the first month and from 15 to 30 cc. in later infancy. The highest values were found in infants receiving artificial food.

Amylase and lipase are always present at birth, and the amounts increase rather rapidly, large quantities of amylase being present after the addition of starch to the food. Only a trace of trypsin is present at birth. The lipase and amylase of the blood serum were also studied. There was found to be no clear parallelism between the amounts of these enzymes in the blood and the amounts in the pancreatic juice.

LESLIE, Evanston, Ill.

ISO-AGGLUTINATION BY HUMAN MILK AND THE REACTION OF CANDIDO. F. FERRARO, Riv. di clin. pediat. **28**:123 (Feb.) 1930.

Candido claimed that the milk of a syphilitic mother agglutinated the blood cells of a healthy person. The author refutes this observation and demonstrates that the milk and blood serums of the same woman have the same agglutinating power toward red blood cells. Milk follows the law of blood grouping. The milk of syphilitic mothers has no specific agglutinating properties that can be ascribable to the disease.

HIGGINS, Boston.

PNEUMOCOCCI IN CHILDREN. A. FOÀ, Riv. di clin. pediat. **28**:134 (Feb.) 1930.

Twenty-four cultures of pneumococci isolated from the sputum of babies with pneumonia were grouped; 17 per cent were of group I, 42 per cent of group II, 8 per cent of group III and 33 per cent of group IV.

Eighty-two per cent of the cultures fermented inulin. Several of the cultures did not dissolve in pure bile, until electrolytes (sodium chloride) were added.

HIGGINS, Boston.

HORMONES AND BREAST SECRETION. G. ABRAHAM, Med. Klin. **26**:164 (Jan. 31) 1930.

Two preparations of hormones of the ovaries and testicles were used in the experiments. The injections were given daily in doses of 1 cc. over a period of ten days. The results of the experiments show that the hormone of the ovaries stimulates the secretion of colostrum, especially in young infants of both sexes. Through daily injections the secretion can be kept up and can be reproduced after cessation of secretion through repeated injections. The ovarian hormone does not increase the normal breast secretion. In a wet nurse with an accessory breast, however, it produced a secretion of typical colostral milk. In two male infants it was possible to produce a secretion by testicle hormone, while others did not show any reactions.

ZESTAY, St. Louis.

STUDIES OF THE ACID-BASE METABOLISM OF THE ORGANISM WITH PARTICULAR REFERENCE TO THE URINE: I. THE HYDROGEN ION CONCENTRATION AND THE AMMONIA COEFFICIENT OF THE URINE. O. SATKE and R. BARTOLOMEY, Wien. Arch. f. inn. Med. **20**:121 (April 5) 1930.

The authors report the minimum and maximum values of the p_H in twenty-four hour specimens of urine. In normal cases it was from 4.7 to 7.1; in renal disease, from 4.7 to 8.4; in febrile diseases, from 4.9 to 7.3; in diabetes, from 4.9 to 6.2; in cardiac disease, from 4.2 to 7.3; in disease of the liver, from 4.8 to 7.0; in gastric disease, from 4.7 to 8.3, and in tetany, from 5.5 to 7.1.

According to Hasselbach, there is a definite correlation between the p_H and the ammonia coefficient. A rise in p_H results in the fall of the ammonia coefficient.

Some authors have found that this does not hold for all cases. The authors believe that for practical purposes it is sufficient to determine whether the ammonia coefficient is normal, increased or lowered.

Increased excretion of ammonia in the urine is not necessarily presumptive evidence of a state of acidosis.

SCHLUTZ, Chicago.

EXPERIMENTAL MEASLES IN RABBITS. P. BELIKOFF, P. P. DWIJKOFF and E. TRUSCHINA, Zentralbl. f. Bakteriol. **112**:78, 1929.

The authors injected rabbits with blood and filtrates of the pharyngeal mucosa from patients ill with measles, and in some instances fever, slight leukopenia and mucosal and skin reactions appeared. Similar results were also observed subsequent to the injection of a pure culture of a diplococcus recovered from patients with measles. Inflammation was found around the blood vessels with proliferation of the adventitial elements frequently mixed with polymorphonuclear leukocytes. These changes were most marked in the skin; to a lesser degree in the larynx and trachea with, at times, hemorrhages in the mucosa. These changes were not observed following the injection of blood and mucosal filtrates from patients free from measles. Several photographs illustrate the changes.

CANNON, Chicago.

THE SCARLATINOTOXIC PROPERTIES OF HEMOLYTIC STREPTOCOCCI FROM CASES OF ANGINA. W. GRUNKE and E. BARTH, Ztschr. f. Hyg. u. Infektionskr. **110**:738, 1929.

Filtrates were made of cultures of hemolytic streptococci obtained from the throats of twenty-one patients with angina lacunaris or angina phlegmonosa. These were compared with standard Dick toxin by skin reaction in thirty-seven persons. In 50 per cent of the cases the skin reaction was identical.

OPHÜLS, San Francisco.

EPIDEMIOLOGIC RESEARCHES IN THE INFANT'S HOSPITAL. R. NEUMANN and H. HAPPE, Ztschr. f. Kinderh. **48**:349, 1929.

Neumann and Happe, who sought to find which factor caused increased morbidity in infants in an institution, were interested also in the question of how long any bacterium stays in a hospital, and how quickly and to what extent it is spread from one child to another. Hemolytic streptococci and the bacillus of diphtheria were used as test organisms. On admission to the hospital, from 92 to 99 per cent of the infants had neither organism; three days later, however, the nasopharynx of 8.3 per cent of the group showed hemolytic streptococci, and 1 per cent showed the Klebs-Löffler bacillus. Three weeks later the percentage had risen to 9.6 and 3 per cent, respectively. In three months the figure in the first instance was doubled and in the second instance it was increased fivefold. Of the infants who remained in the hospital for thirteen weeks and longer, two thirds showed the

presence of streptococci and one third, diphtheria. Germs that have reached the nasopharynx stay for one week in 38 per cent; they remain for four weeks in 58 per cent of the cases if the organism is hemolytic streptococcus and in 15 and 30 per cent of the cases, respectively, if the organism is that of diphtheria.

EMERSON, Boston.

FURTHER STUDIES ON GRIP, IN RELATION TO A NEW EPIDEMIC OF INFLUENZA VERA IN THE CHILDREN'S CLINIC OF THE UNIVERSITY OF HALLE IN THE WINTER 1928-1929. E. BARTH and M. HAHN, Ztschr. f. Kinderh. **48**:360, 1929.

The frequent demonstration of *Bacillus influenzae* justified the recognition of the epidemic as one of influenza vera. The Pfeiffer bacillus was brought into the clinic by children infected with grip, from which the ward personnel was infected. There were no complications among the adults, but four of ninety-four babies died of bronchopneumonia; the sputum in these cases yielded *Bacillus influenzae* in almost pure culture.

EMERSON, Boston.

IMMUNOBIOLOGY OF SCARLET FEVER: II. THE CALCIUM EXTINCTION PHENOMENON. H. BAAR, H. BUFF and L. SZÉKELY, Ztschr. f. Kinderh. **48**:384, 1929.

In spite of great similarity, the mechanisms of the serum and the calcium extinction phenomenon are different. In the conflict of views on the primary toxic or allergic nature of scarlet fever, the discovery of the calcium phenomenon is an argument neither for nor against this theory. In no case is it allowable to conclude from the power of a substance to cause extinction, as to its content of antibodies, especially of antitoxin. The assumption that the capacity of the Dick serum to cause extinction stands in causal relation to its capacity to suppress the Dick reaction must first be proved. The experiments of Groer, Cook and more recently Tezner have shown that the basis of the Dick scarlet fever theory is not sound. On the other hand, it must be emphasized that the direct evidence for the allergic nature of scarlet fever and of the Dick reaction still stands. The most weighty support that remains is the eosinophilia and the hastened type of eosinophilic reaction at the onset of the disease. The authors have taken the trouble to test the allergic nature of the Dick toxin in the Prausnitz-Küster experiment. Children giving a negative reaction to the Dick test, older persons, who regularly possess a neutralizing serum, and young infants who usually give a negative Dick reaction and who possess no antitoxin in the serum, were given an intracutaneous injection of 1 cc. of serum obtained from children giving a positive Dick reaction; after twenty-four hours the Dick test was repeated on the same areas. In no case could a transference of sensitiveness to the Dick test be established. It is further remarkable that it could not be produced in guinea-pigs, either by previous treatment with bouillon, with scarlet fever or with erysipelas streptococci.

EMERSON, Boston.

THE RESISTANCE OF SKIN CAPILLARIES IN RHEUMATIC DISEASES OF THE HEART. IRMA SIMON, Ztschr. f. Kinderh. **48**:437, 1929.

The rheumatic endocarditides are accompanied frequently by a diminished resistance of the capillaries to negative pressure; chronic and septic forms of heart disease show that the phenomenon occurs almost without exception and often in a pronounced manner. No conclusions as to diagnosis or prognosis can be drawn from the results of the cupping reaction described in this article, as individual, normal differences vary widely and as even healthy children give positive results in a high percentage of cases. The figures given by Simon agree closely with those obtained by Schour in testing for the related Rumpel-Leede sign.

EMERSON, Boston.

Nutrition

SUNLIGHT TYPE S-1 LAMP (G. E.) THERAPY IN HUMAN RICKETS AND RACHITIC SPASMOPHILIA. HENRY J. GERSTENBERGER and G. R. RUSSELL, J. A. M. A. **94**:1049 (April 5) 1930.

Observations were made on the efficacy of the Sunlight Type S-1 Lamp of the General Electric Company in the treatment for rickets. Weekly erythema-producing exposures of both the front and the back surfaces of the body of three rachitic infants to the rays produced by this lamp brought about healing observed roentgenologically and in the blood within the time previously established by the authors in similar exposures to the quartz lamp.

BONAR, Salt Lake City.

COMPARATIVE VALUE OF VIOSTEROL AND COD LIVER OIL AS PROPHYLACTIC ANTIRACHITIC AGENTS. ADOLPH G. DE SANCTIS and JOHN DOBSEY CRAIG, J. A. M. A. **94**:1285 (April 26) 1930.

In a comparative study of the value of viosterol and cod liver oil in the prevention of rickets the authors found that 3 teaspoonfuls of cod liver oil daily prevented rickets in 97 per cent of 100 cases, while viosterol 100 D, 10 drops daily, prevented rickets in 77 per cent of 123 cases. In the present recommended dosage viosterol is less effective than cod liver oil in the prevention of rickets. In this series the infants given viosterol received about twice as many rat units of vitamin D as did the infants given cod liver oil. Therefore, the present recommended prophylactic dose of viosterol is too small to prevent rickets, or the disease is not due entirely to a deficiency of vitamin D. The authors lean toward the latter view.

BONAR, Salt Lake City.

NEWER ASPECTS OF THE THERAPEUTICS OF VIOSTEROL. (IRRADIATED ERGOSTEROL). A. F. HESS, J. M. LEWIS and H. RIVKIN, J. A. M. A. **94**: 1885 (June 14) 1930.

In its present dosage viosterol confers protection against rickets. Some evidences of this disorder, however, were apparent in a small number of cases in which viosterol was given. No hypercalcemia or other untoward symptoms were apparent. The cases showing mild rickets maintained a normal phosphorus balance, which indicated that when viosterol is being given the presence of rickets must be determined by clinical signs and roentgenograms. Viosterol has a remarkably curative effect on rickets, is reliable, has quick action and is not associated with the development of hypercalcemia. The dosage should be increased from two and one half to three times, which can be best accomplished by increasing the strength of the solution. The author suggests a better method of standardizing the preparation.

BONAR, Salt Lake City.

VIOSTEROL (IRRADIATED ERGOSTEROL): PROPHYLACTIC AND THERAPEUTIC DOSAGE. JULIUS H. HESS, H. G. POSCHER, M. L. DALE and R. I. KLEIN, J. A. M. A. **95**:316 (Aug. 2) 1930.

From an extensive study the authors conclude that for the average normal infant from birth to 1 year of age, under varied environmental and seasonal conditions in the temperate zones, 10 drops of viosterol in oil a day is a minimum dose for prophylaxis. Its administration should be started in the first weeks of life. In a small group of cases studied the average time required for demonstration of healing was about twenty-eight days. Mild rickets healed following the administration of from 10 to 15 drops of viosterol daily, while infants with severe rickets needed as much as from 30 to 60 drops. Massive doses of viosterol in oil failed to cause toxic symptoms in any of the infants during the period of investigation. Apparently there is a large factor of safety in the administration of large doses of viosterol in infants.

BONAR, Salt Lake City.

THE DOSAGE OF ULTRAVIOLET RADIATION IN INFANTS WITH TETANY. HARRY BAKWIN and RUTH MORRIS BAKWIN, J. A. M. A. **95**:396 (Aug. 9) 1930.

The authors studied the effect of measured amounts of ultraviolet radiant energy on the serum calcium of twenty-eight infants with tetany. There is an optimal range of dosage above which and below which the rate of rise of the serum calcium is slowed. A daily dosage of two minutes' exposure of the front surface of the body and two minutes' exposure of the back surface at 50 cm. is optimal unless the burner is deteriorated. With optimal dosages the rise of serum calcium in white and Negro infants with tetany is about the same, although the minimal dosage necessary for cure is greater in Negro than in white infants.

BONAR, Salt Lake City.

ROUTINE COMPLEMENTARY FEEDING OF THE NEW BORN. J. E. TOOTHAKER, Northwest Med. **29**:158 (April) 1930.

Comparing 100 infants given complementary feedings from the time of birth with 100 infants not given the feedings, Toothaker reports the following results: Of those given complementary feedings, 88 were solely breast fed when they left the hospital; only 72 of the other infants were solely breast fed. Those of the infants given complementary feedings who regained their birth weight (82 per cent of the group) did so in an average of 7.7 days. Of the other infants only 68 per cent regained their birth weight during the routine stay of from twelve to fourteen day; these regained it in an average of 9.8 days. Complementary feeding reduced the incidence of acute inanition, as only 2 per cent of the infants given complementary feedings were affected, while the usual incidence of 11 per cent was found among those not receiving the feedings.

SCOTT, Philadelphia.

PYLOROSPASM OF INFANTS: A TENTATIVE METHOD FOR CONTROL OF THE VOMITING. D. M. DAYTON, Northwest Med. **29**:163 (April) 1930.

Dayton reports two cases in which phenobarbital sodium was given as follows: one-fourth grain (16.2 mg.) every four hours until the infant was continuously drowsy. If the patient vomited, the full dose was immediately repeated, but if he was too drowsy to nurse well the next dose was omitted. The results were favorable.

SCOTT, Philadelphia.

VEGETABLE PROTEINS IN INFANT FEEDING. L. RIBADEAU-DUMAS, RENÉ MATHIEU and L. WILLEMIN, Nourrisson **18**:165 (March) 1930.

The history of the rôle of soy bean flour in the feeding of infants is reviewed; the work of the American investigators in this field is especially emphasized. The analyses of the protein amino-acid figures are quoted from the articles of Hill and Stuart. These show that soy bean flour furnishes all the nitrogen products necessary for complete nutrition and growth. The formula of sobee is given in detail.

The authors have found soy bean preparations useful in the treatment for both the ordinary and the parenteral types of dyspepsia as encountered in infants, but they place most emphasis on the usefulness in cases of milk idiosyncrasy and in cases of infantile eczema.

Attention is directed to the fact that soy bean flour concoctions have a peculiar taste which makes them inacceptable to some infants. Further, the weight curves of infants dependent on soy bean preparations as their only source of protein are often unsatisfactory.

MCCLELLAND, Cleveland.

HOW THE PATHOGENESIS OF RICKETS IS RECONCILED WITH ITS ETIOLOGY. V. ZAMORANI, Riv. di clin. pediat. **28**:89 (Feb.) 1930.

The author revives the theory of Pacchioni that rickets is caused by an alteration of the physicochemical structure of the living tissue so that its capacity to fix the phosphate-ion is diminished.

HIGGINS, Boston.

METABOLISM STUDIES WITH ACID MILK. M. NIERMANN and M. WINTER, Arch. f. Kinderh. **89**:290 (Feb.) 1930.

Citric acid milk was concluded to be the best acid milk for children. The body mineral balance was best maintained on this. After seventy days there were no clinical signs of rickets in children fed this milk exclusively.

SANFORD, Chicago.

ANTIRACHITIC VALUE OF IRRADIATED FRESH COW'S MILK. H. BRÜHL, Med. Klin. **26**:509 (April 4) 1930.

Fresh milk was irradiated in an apparatus of Scholl's and was supplied every morning in fresh condition. Sixteen children with different degrees of rickets were used in the experiment. The same milk also was used in experiments on rats. The results of this work show that the irradiated milk had only a slightly slower curative effect on rickets than quartz light or viosterol. The antirachitic factor is present in sufficient quantity so that the amount needed is not too large. No untoward effects have been noted. In more serious forms of rickets or in case of complications, it seems to be better to use viosterol or quartz light. Under those circumstances a large amount of milk, as it would be needed, seems to be contraindicated; it is also desirable that cure should be attained in a short time. In prophylaxis of rickets, on the other hand, irradiated milk seems to be the method of choice.

ZENTAY, St. Louis.

CONGENITAL ANOMALIES OF LIPOID METABOLISM. A. ABRIKOSSOFF and H. HERZENBERG, Virchows Arch. f. path. Anat. **274**:146, 1929.

The so-called Christian type is not a disease by itself but a skeletal form of Niemann-Pick's disease. All congenital anomalies of lipoid metabolism (xanthoses) form one group. The anomaly may be more marked in the cholesterol metabolism, in the neutral fats, the phosphatides or the kerasin. There may be ectodermal, visceral or skeletal forms. These anomalies obviously are mutations. They represent an inherited genotypically fixed disease of the mesenchyme. The factors are recessive and become manifest only after inbreeding. The hypercholesterinemia is not primary.

PLAUT, New York.

REMARKS ON ARTICLE BY ABRIKOSSOFF AND HERZENBERG. L. PICK, Virchows Arch. f. path. Anat. **274**:152, 1929.

The three types, Gaucher's disease, Niemann-Pick's disease, and the disease described by Christian, are different manifestations of a primary disturbance of lipoid metabolism. Nevertheless, each of the three is a definite clinical and anatomic entity. The clinical course of Niemann-Pick's disease generally is too fast for the development of a skeletal form. Intermediate forms must be expected. So far, about fifty cases of Gaucher's disease are on record and about fifteen of morbus Niemann-Pick and Christian's syndrome. In comparison with these figures, the number of intermediate forms is negligible.

PLAUT, New York.

CLINICAL EXPERIMENTAL STUDIES ON WHEY SUGAR FEVER. JOHANNES JOCHIMS, Ztschr. f. Kinderh. **48**:371, 1929.

The author refers to a partial contradiction that arises from the researches of Finkelstein and of Hirsch and Moro concerning the pyrogenic factors in whey sugar fever. It concerns the evaluation of albumin-free whey residue. According to Finkelstein, sugar, albumin and albumin-free whey residue are responsible in equal measure for the origin of this fever, whereas according to Hirsch and Moro, albumin-free whey residue plays no rôle. An explanation of the contradiction is significant in the general theory of alimentary fever.

The chemical study of albumin-free whey by Finkelstein gave regularly a content of about 0.45 per cent albumose, including a fraction of a peptone-like body, while Hirsch and Moro, who used another method, found no such product of high protein cleavage.

The the content of albumose is decisive for the outcome of the research and responsible for the alimentary fever in the technic of feeding used by Finkelstein has been demonstrated by corresponding researches in feeding. In close agreement with Finkelstein, the following fact was demonstrated. By adding 0.45 per cent albumose, corresponding to the natural albumin-free whey, to the milk sugar plasmon food (14.5 per cent milk sugar, plus 3.5 per cent plasmon in water) used by Finkelstein as a nonpyrogenic control food, one produces an alimentary fever. There is no evidence of a pyrogenic action of whey salts. The whey sugar fever is accordingly referred to the pyrogenic action of sugar plus protein or the high product of protein cleavage. Albumose and similar products seem to have a special significance.

EMERSON, Boston.

THE PHYSIOLOGY OF DIGESTION IN INFANTS: THE DIGESTION OF ALBUMIN IN THE INTESTINE. O. BUDDE and E. FREUDENBERG, Ztschr. f. Kinderh. **48**: 390, 1929.

It was established that the protein of human milk is more resistant to digestion by trypsin than the protein of cow's milk, a resistance that can be traced to the content of albumin. In consideration of the establishment of this fact and of the demonstration of the small production of ferments in the breast-fed baby, it seems plausible that the albumin in human milk is absorbed before it is completely broken down.

EMERSON, Boston.

Diseases of the New-Born

VARIX OF THE UMBILICAL CORD. FRED L. ADAIR and R. E. MCDONALD, Am. J. Obst. & Gynec. **17**: 836, 1929.

The case reported is one of ruptured umbilical varix and adds one to the four cases which the authors found recorded.

KOBAK, Chicago.

RESPIRATORY DISEASES OF THE NEW-BORN. ALVIN E. SIEGEL, Arch. Pediat. **46**: 730 (Dec.) 1929.

Complete expansion of the lung does not occur for a number of days after birth. In premature and frail babies, it is delayed even more. Respiratory movements are at first diaphragmatic, later gradually becoming thoracic. Atelectasis is physiologic and temporary during the first few days of life. Asphyxia neonatorum is the earliest pulmonary condition met with in the newly born. It may be intra-uterine (congenital) or extra-uterine (acquired). There is a detailed description of these types of asphyxia. Intracranial birth trauma gives rise to respiratory symptoms, as do also congenital defects of the upper respiratory passages, infections, syphilis, adenoids, etc. Laryngismus may be due to a spasmophilic tendency or to abnormality of the thymus gland. The degree of enlargement of the thymus gland appears to bear no relation to the severity of the symptoms of the disorder. Abnormalities of the bronchi and lungs may also give rise to respiratory difficulties. Atelectasis is the most frequent pulmonary condition seen in the newly born. Hypostatic congestion is occasionally seen. Inflammatory diseases of the lungs may result from intra-uterine infection or later. Emphysema is sometimes seen. Diaphragmatic hernia may result in respiratory difficulty. A case of thymus gland disease and one of atelectasis is reported.

WILSON, Norfolk, Va.

THE BLOOD PLATELETS IN NEW-BORN INFANTS. JULIUS JARCHO, Arch. Pediat. **47:** 230 (April) 1930.

The writer studied platelet counts and coagulation and bleeding time in 100 new-born infants. He reviews the literature on this subject. Most of the counts were made within twenty-four hours after birth, and none later than forty-eight hours after birth.

The platelet counts varied from 78,740 to 500,000. Five infants showed counts below 100,000, and ten counts over 300,000. The majority of cases showed counts between 150,000 and 250,000. Bleeding time and coagulation time were found to be within the limits of normal.

There appeared to be no correlation between the platelet count and the red cell count.

WADDELL, University, Va.

CASE OF SCLEREMA NEONATORUM. E. CONDON, Brit. M. J. **1**:443 (March 8) 1930.

The infant was born prematurely, while the mother was suffering from pneumonia. It is interesting to note that though the mother made a rapid recovery, lactation never appeared. The infant died in a few days.

RATTNER, Chicago.

SPINA BIFIDA (TWO OTHER CASES IN SAME FAMILY). BERNARD MYERS, Proc. Roy. Soc. Med. **23**:603 (March) 1930.

An infant, aged 9 weeks, suffered from meningo-myelocele in the lumbo-sacral region, and a steady increase of the circumference of the head. There were four in the family, including girl twins both of whom had spina bifida and died in the first week of life.

WILLIAMSON, New Orleans.

CRYING AS A MEANS OF RESPIRATORY GYMNASTICS IN THE NEW-BORN. J. PESCHER, Presse méd. **38**:301 (March 1) 1930.

The author points out the damage that may result from imperfect aeration of the lungs in the new-born. He advocates daily exercises of crying to strengthen the respiratory apparatus. These so-called exercises consist of causing the infant to cry for a definite time each day at the same time. The periods of crying are increased each day as the infant grows stronger.

SANFORD, Chicago.

ANEMIA PROPHYLAXIS IN THE NEW-BORN. O. ULMER, Arch. f. Kinderh. **89:** 272 (Feb.) 1930.

As a prophylaxis against the anemia that develops in premature infants, the author uses iron therapy. Six cases are tabulated in which both the erythrocytes and the hemoglobin were kept up to a normal standard by this method.

SANFORD, Chicago.

THE FATE OF THE NEWLY BORN INFANTS BORN TO MORPHINE-ADDICT MOTHERS. L. LANGSTEIN, Med. Klin. **26:** 500 (April 4) 1930.

Apparently there is decided damage done to the fetus of mothers who are morphine addicts. Clinical signs are to be found in the newly born baby. The most frequent manifestation is a severe restlessness and irritability shortly after birth. Newly born babies of this type should be treated in a hospital only, because during the first few weeks there is usually a serious nutritional disorder. The author advises reduced feeding with breast milk or possibly with centrifugated breast milk. Opium may be needed to overcome the restlessness.

ZENTAY, St. Louis.

THE SIGNIFICANCE OF THE PLACENTAL CIRCULATION FOR THE MAINTENANCE OF THE HEART ACTION IN THE NEW-BORN. H. SCHUMACHER, Munchen. med. Wchnschr. **77**:317 (Feb. 21) 1930.

Schumacher reports an interesting observation in a spontaneous abortion at five months. The fetus and placenta were expelled together and the cord was not tied. There were no respiratory attempts and no effort made to induce respiration. The heart action, however, persisted for fifty minutes after delivery, and the blood vessels in the cord and placenta did not collapse during this period.

BRAHDY, Mount Vernon, N. Y.

HYPOPLASIA OF CORPUS CALLOSUM IN NEW-BORN INFANTS. HEINRICH V. HAYEK, Virchows Arch. f. path. Anat. **273**:767, 1929.

The corpus callosum was half the normal size. The brain had been fixed in situ. The gyrus cinguli was interrupted and thin, corresponding to the absence of corpus callosum fibers. There were no other important anomalies.

PLAUT, New York.

IS THERE GREATER RESEMBLANCE BETWEEN DIZYGOTIC THAN MONOZYGOTIC TWINS WITH REFERENCE TO WEIGHT AND LENGTH? ERIK ESSEN-MÖLLER, Acta obst. et gynec. Scandinav. **9**:107, 1930.

All authors do not agree that monozygotic twins resemble each other in length and weight more closely than do dizygotic twins. The author has examined 497 twins, all of whom were alive at the beginning of labor and has correlated the measurements. He was unable to determine whether or not there was a closer correlation of weights in the monozygotic than in the dizygotic twins.

The dizygotic twins have a greater average weight and length than the monozygotic. There is a closer correlation of length between the monozygotic than between the dizygotic twins, and consequently they are more nearly alike in this regard. There is as much correlation between male and female as between the same sexes of dizygotic pairs.

The sex differences in length and weight between members of opposite sexed pairs is less than between dizygotic male and female pairs.

ADAIR, Chicago.

RUPTURE OF THE LIVER IN THE NEWLY BORN. SUSE GESELL, Acta obst. et gynec. Scandinav. **9**:180, 1930.

The author reports three of four cases of rupture of the liver in the newly born found in the literature and adds three of his own.

Two of these cases occurred in fully developed infants born to the same mother and dying of ruptured livers. The author believes that the opinion that there is an essential difference between subscapsular hemorrhage and parenchymatous rupture cannot be sustained.

The author feels that in the aforementioned cases, in which the mother had an obliquely contracted pelvis, there was a combination of abdominal compression and violence working at a tangent to the fetal abdomen.

The author believes that there may be other causes, such as temporary alterations in the bleeding and coagulation time of the blood—pseudohemophilia. He is of the opinion that there may be two factors, a mechanical traumatic and a constitutional one.

ADAIR, Chicago.

SYSTEM OF PLANTAR CLASSIFICATION FOR THE NEWLY BORN. EMIL JERLOV, Acta obst. et gynec. Scandinav. **9**:267, 1930.

The author bases his classification on a study of 450 cases at Halsingborg's Maternity Hospital.

This system is based on the designs alone and is limited to those on the big toe and in the metatarsal region. The design present on the great toe makes up the denominator of a fraction and that of the underlying metatarsal portion the numerator.

The author follows Galton's system of nine different kinds of designs, arches, tented arches, loops, etc.

In the metatarsal region he finds three different varieties of loops which give ten designs for this region. This gives 90 main groups. Subgroups are formed from the designs on the lateral metatarsal regions.

ADAIR, Chicago.

INTRATHORACIC AND INTRA-ABDOMINAL HEMORRHAGES IN THE NEWLY BORN. BIRGER LUNDQUIST, Acta obst. et gynec. Scandinav. **9**: 331, 1930.

The author collected 52 cases in only 3 of which were there intrathoracic hemorrhages; 1 of uncertain origin in the mediastinum and the other 2 from the thymus. Of the 49 cases of intra-abdominal hemorrhages, 5 were from parenchymatous rupture of the liver, 14 were subcapsular liver hemorrhage, 18 suprarenal bleeding, 1 splenic rupture and 12 intraperitoneal hemorrhage of unknown origin.

Of the etiologic factors one must consider the disturbed fetal circulation from the labor itself, the altered fetal circulation at birth, traumatic and mechanical conditions, and infections such as syphilis, asphyxia and hemophilia.

Most of the infants who survived the first twelve hours died rather suddenly without presenting any physical signs.

ADAIR, Chicago.

A STUDY OF THE TYPE OF RESPIRATION OF PREMATURE INFANTS. T. SALMI and E. E. VUORI, Acta paediat. **9**:432, 1930.

The respiratory movements were studied by encircling the infant's chest, or in some cases the abdomen, with an inflated tube of soft rubber and recording the alterations of gas pressure on a smoked drum. Most of the measurements were made with the infant quiet or asleep, after a meal. Twelve of thirteen infants studied showed at some time Cheyne-Stokes' breathing, though in three of them it was not entirely typical. Premature infants are most likely to show Cheyne-Stokes' respiration in the early days of life, during illness, when asleep and following hot baths. The more immature such an infant is, the longer does the tendency to spells of this type of respiration persist. As a general rule, this tendency lasts through the first month or two of life.

MCINTOSH, Baltimore.

TEMPERATURE REGULATION AND LEUKOCYTOSIS IN PREMATURE INFANTS: THE EFFECT OF WARM BATHS. INKERI KIJANEN and LEA HIETARINTA, Acta paediat. **9**:444, 1930.

After a control observation of rectal temperature and leukocyte count, an infant was placed for from five to twenty minutes in a warm bath. He was then put back in the crib, clothed but without an external source of heat, and the observations repeated at intervals of ten or twenty minutes until the values returned to the starting level. The temperature of the bath water varied from 39 to 43 C. (102.2 to 109.4 F.), and caused an elevation of from 0.8 to 3.2 C. (0.9 to 5.7 F.) in the infant's temperature between the first two readings. The observations indicated a diminishing thermolability with increasing age. The procedure caused in some infants a rise, and in others a drop, in the white blood cell count.

MCINTOSH, Baltimore.

A CASE OF CONGENITAL ATRESIA OF THE BILE DUCTS. V. I. BAASTRUP, Acta paediat. **9**:509, 1930.

An infant became definitely jaundiced at the end of the first week of life, and the color increased progressively. She was admitted at 2½ months of age and

presented the classic picture of complete obstructive icterus. At an exploratory operation the gallbladder and visible bile ducts appeared normal (it is not stated whether the gallbladder contained bile) and the liver was enlarged, firm and bluish black. A piece of liver removed at this time showed interlobular fibrosis with round cell infiltration and pseudobile duct formation. The patient died at a little less than 6 months of age. Autopsy was not permitted.

McIntosh, Baltimore.

Acute Infections

Lesions of Fowl-Pox and Vaccinia. C. Eugene Woodruff, Am. J. Path. **6**:169, 1930.

The histology of lesions obtained in chick epithelium following inoculation with vaccinia virus alone, fowl-pox alone and the two viruses mixed is described. The characteristic virus bodies of fowl-pox, whether occurring in the skin or the cornea of the chick, give a positive reaction for fat. The Guarnieri bodies of vaccinia do not stain for fat. Ludford's statement regarding the identity of the virus bodies of vaccinia and fowl-pox in the chick is refuted. His observations are due, it is believed, to the utilization of tissue from a mixed lesion of fowl-pox and vaccinia.

Author's Summary.

Staphylococcic Septicemia: Report of a Case with Complete Recovery. Ivan W. Woolley, Arch. Pediat. **46**:741 (Dec.) 1929.

In a well nourished and well developed girl, aged 5, a blood stream infection with *Staphylococcus albus* developed after she had been knocked down by another child. Pus was aspirated from the left hip joint and from the right side of the chest. Multiple superficial abscesses later developed in various parts of the body. These were incised and drained. Osteomyelitis of the right thigh developed. At operation, a major portion of the lower one third of the bone was removed. An autogenous vaccine was given; also ultraviolet light, cod liver oil and a parathyroid preparation with calcium lactate. Nuclear extract was employed, apparently with good results, and the patient made a complete recovery after about a year.

Wilson, Norfolk, Va.

A Further Report on the Treatment of Whooping Cough by Intramuscular Injections of Ether. Julius Levy and A. S. Finkelstein, Arch. Pediat. **46**:762 (Dec.) 1929.

One hundred and four patients were treated at the City Dispensary, Newark Department of Health between May and August, 1929. Intramuscular injections of ether in oil were used. The ages varied from 10 months to 2 years. In 24 per cent the condition was improved, in 22 per cent unimproved and in 4 per cent slightly improved. Ninety-four patients received 1 cc. of ether in 1 cc. of oil; ten received double this dose. There was no abscess or necrosis at the site of injection. The skin was cleansed with 5 per cent tincture of iodine, washed off with 95 per cent alcohol; the injection was given in the buttocks. No other medication was given. In the colored patients there was absorption after from forty-eight to seventy-two hours, whereas in the white children the absorption occurred within twenty-four hours. The patients who showed improvement were given from four to seven doses, while those who showed none received from four to eleven doses. The duration of the illness at the time of the first injection was from two to twenty-one days. The authors suggest further study of the method, employing double the dose, and they add that they feel that the treatment offers a definite means of aiding the child with whooping cough. Illustrative cases are given.

Wilson, Norfolk, Va.

A Skin Test for Susceptibility to Smallpox. Sanford B. Hooker, J. Infect. Dis. **45**:255, 1929.

Epidermal injections of heat-killed vaccine virus produce definite and easily interpretable reactions which are rather highly dependable as indexes of immunity to smallpox, correlating well with the various grades of response to living virus. The few discrepant reactions have been on the "false" positive side and are probably ascribable to other proteins which contaminate crude virus; the negative reaction as a criterion of susceptibility has so far been wholly reliable.

Author's Summary.

The Leukocytosis in Scarlet Fever in Relationship to Serum Treatment and Complications. Margaret E. Wylie, J. Infect. Dis. **45**:408, 1929.

The leukocyte count is a less reliable index of the severity of scarlet fever than is the general clinical picture and can seldom be used as an index of the severity or of the progress of a case of scarlet fever with respect to the probable onset of complications. In uncomplicated and complicated cases of scarlet fever a pronounced fall in the white cell count, between the first and third day, is a constant finding. There is no evidence to indicate that the administration of antitoxin in cases of scarlet fever has any effect on the leukocyte count from admission to the seventh day of illness. In cases of scarlet fever a polymorphonuclear leukocytosis is the rule, but the excess of polymorphonuclear cells is slight, and their proportion does not undergo much variation throughout the course of the disease nor does it differ characteristically in the complicated and uncomplicated cases. The behavior of these cells does not distinguish the simple from the complicated cases. From the first day onward the small lymphocytes undergo a steady and constant increase. The large lymphocytes increase from the first to the third day but decrease thereafter until by the seventh day their original level is virtually regained. This constant curve is independent of the occurrence on nonoccurrence of complications and of the giving or withholding of serum.

Author's Summary.

Herpes Ophthalmicus Coincident with Varicella in Adults. B. Barling and John Cahill, Brit. M. J. **1**:823 (May 3) 1930.

Two cases were cited. One was in a man, aged 69; the other occurred in a man, aged 80. Neither patient had ever had chickenpox. There was no history of previous exposure.

Rattner, Chicago.

The Mechanism of a Measles Epidemic. Percy Stocks, Lancet **1**:790 (April 12) 1930.

From the author's figures derived from the St. Pancras study and those from Butler's series he concludes that in the second and third years of life the expectation of catching measles during an epidemic for a child who has not had it is increased sixfold if a case occurs in the same house, and that at the ages 4, 5 or 6 years it is increased five-fold.

The beginning of an epidemic is given as follows: "It is just as though we kept on day after day inoculating a bacterium into a liquid culture medium to which some essential constituent, x, lacking to start with, is also being daily added in successive small quantities. No growth at all will occur until a critical concentration of x has been reached. This, I think, is the best explanation of the sudden rise of true infectiousness which precedes the onset of an epidemic in most diseases I have studied, and in saying that I admit it is nothing but Gill's 'quantum' theory stated in such a way as to make it rather easier to visualize."

The author explains the biennial periodicity of measles epidemics on the theory that each case of measles is accompanied by several latent cases but that the latent immunity so produced gradually disappears after the epidemic, taking about two years instead of five as Gill has shown to occur in malaria. "We must hope for either a simple method of inoculation which will produce a more or less permanent immunity or else a simple method of rendering an attack abortive and harmless, such as the proposed method of inoculating contacts with their parents blood, whilst at the same time allowing it to produce a permanent immunity."

LANGMANN, New York.

PRODROMAL RASHES. ELIOT SWAINSTON, Practitioner **124**:520 (May) 1930.

In some of the eruptive fevers, rashes occur during the prodromal period. Owing to the inconstancy of their appearance, instead of being a help in diagnosis they often are a source of confusion or error. The author feels that these early rashes are probably caused by a generalized toxemia.

Prodromal rashes are sometimes noted in the following diseases: In chickenpox the rash most usually seen resembles scarlet fever. The scarlet rash may be distinct and generalized. The distinction between it and a true scarlet fever rash is entirely a matter of degree. The examination of the tongue and throat usually gives valuable aids to diagnosis. The degree of fever is not of material assistance.

During the prodromal period of measles various blotches, papules or macules may appear in isolated patches on the trunk. The rash resembles a true measles rash but occurs on a much smaller scale. Sometimes, a scarlatiniform rash is observed. The presence of Koplik's spots and a mild coryza are, of course, diagnostic.

In smallpox, the prodromal rashes may be general or local; the former are usually erythematous, patchy or morbilliform and the latter petechial.

Occasionally in epidemic encephalitis (lethargica) a prodromal rash appears, consisting of faint patches of erythema on the trunk or the limbs.

The author emphasizes the importance of a complete inspection of the entire surface of the body, the examination of the buccal mucous membranes and the fauces as well as a careful search for other signs and symptoms in order not to be misled by the peculiarities of the prodromal rashes.

SAFFINGTON, San Francisco.

MENINGITIS AND MENINGO-ENCEPHALITIS IN INFECTIOUS PAROTITIS. R. J. WEISSENBACH, G. BASCH and M. BASCH, Ann. de méd. **27**:5 (Jan.) 1930.

The most common form of meningeal involvement in combination with infectious parotitis is the following: Suddenly all the typical signs of meningitis develop in a child. Lumbar puncture shows a marked cellular reaction without microorganisms. After a few days, usually after from three to six, swelling of the parotid glands settles the clinical diagnosis. The parotid is usually only mildly involved and the meningeal signs disappear after a period of from one to three weeks. In a second group of cases the infection with the unknown micro-organism produces a clinical picture that closely resembles epidemic encephalitis. Vomiting, spasmodic contractures, transitory hemiparesis and oculomotor paresis, combined with meningeal symptoms and a cellular spinal fluid, are reported. The swelling of the parotid again follows the meningo-encephalitis, and all the signs of disease disappear as rapidly as they came. In a third group of cases of meningo-encephalitis the parotid was not involved and the connection of the clinical symptoms with the virus of the parotitis could only be established indirectly by the discovery of typical cases of parotitis in the family or neighborhood of the patient. In some of these observations the region of the parotid was sensitive to pressure, without showing any fluctuation.

An attempt was made to establish an early diagnosis by a careful examination of the cerebrospinal fluid. Following are the characteristics which allow a differential diagnosis from epidemic, tuberculous and syphilitic meningitis: The fluid is clear and sterile. It is not xanthochromic and contains a large number of cells, in most cases more than 100 and up to 1,000 per cubic millimeter. As a rule there are only a few polymorphonuclear cells, most of the cells being lymphocytes (from 63 to 100 per cent). The albumin is only slightly increased; the maximum was 1.42 Gm. per liter. The sugar content is normal, and the chlorides are somewhat diminished. The number of lymphocytes decreases from the maximum to normal within from four to five days.

The sudden onset in a healthy child, the absence of fibrin and the low content of albumin make an early differential diagnosis from tuberculous meningitis possible. Furthermore, in the latter the sugar content of the spinal fluid is always diminished. If parotitis meningitis occurs in an adult, syphilitic meningitis must always be considered first in differential diagnosis. Negative reactions to the Bordet-Wassermann test and the benzoin test are indications against a syphilitic infection, and a differential count of the spinal fluid cells in the latter infection usually reveals more intact polymorphonuclear, large mononuclear and plasma cells than in parotitis. The differential diagnosis from epidemic meningitis is sometimes difficult and can be established only in the later stages of the disease or if an epidemic is present. Meningococcus and other infections of the meninges can be diagnosed by cultures of the fluid, which are sterile in the parotitis infection. If a clear fluid makes diagnosis difficult, the presence of fibrin, the increased albumin and the large number of altered polymorphonuclear cells will help one to recognize these forms.

The favorable prognosis in cases of parotitis meningitis makes an early diagnosis valuable, and the rapid improvement makes therapeutic action unnecessary.

WEIL, Chicago.

EXPERIENCES WITH DIPHTHERIA ANATOXIN. MARCELLE NICOLLE, Arch. Inst. Pasteur de Tunis **19**:55, 1930.

Over a period of eighteen months, 987 persons were given injections of diphtheria anatoxin or toxid, 789 of whom received the full three injections, 0.5, 1.0, and 1.5 cc., spaced respectively at three week and fifteen day intervals. The age group ranged from 1 to 37 years, the younger ages predominating. Following the first injection, low fevers were noted in approximately 1 per cent of the cases, lasting a maximum of three days. Reactions were more marked following the second injection, occurring in some 4 per cent of the persons, with higher temperatures. No reactions were noted after the third injection. Reactions in children under 5 years of age were not observed.

MARSHALL.

A NOTE ON THE TREATMENT OF DIPHTHERIA CARRIERS WITH OXYQUINOLINE SULPHATE. M. LISBONNE, P. DEVÉZE and LABRAQUE-BORDENAVE, Paris méd. **1**:234 (March 8) 1930.

The authors have cleared up diphtheria carriers in from four to eight hours by insufflations twice a day with a powder composed of 1 Gm. of neutral sulphate of oxyquinoline and 100 Gm. of carbonate of bismuth.

SANFORD, Chicago.

ENCEPHALITIS AS A COMPLICATION OF MEASLES. R. DEBRÉ, R. TURQUETY and R. BROCA, Presse méd. **38**:348 (March 12) 1930.

The authors report two cases of measles in children, aged 7 and 8 years respectively, who subsequently had typical encephalitis.

SANFORD, Chicago.

NORMAL AND PATHOLOGIC BEHAVIOR OF ANTIMEASLES IMMUNITY IN THE YOUNG INFANT. A. F. CANELLI, Rev. franç. de pédiat. **5**:668 (Dec.) 1929.

After discussing the immunologic factors probably responsible for the rarity of measles during the first six months of life, the author reports two cases of measles in very young infants. The first occurred during an epidemic in an infant aged 3 weeks, neither of whose parents gave a history of having had measles. In the second infant, aged 5 weeks, both parents gave a definite history of measles. The first case follows normally the laws of immunity; the second does not and is designated by the author as pathologic in this respect.

There is also a discussion of congenital measles, and suggestions are given as to the best method of preparing the serum of patients convalescing from measles.

LESLIE, Evanston, Ill.

SMALLPOX VACCINATION AND TETANUS. MARTINEZ VARGUS, Med. de los niños **31**:1 (Jan.) 1930.

Several cases of tetanus and the various means by which each patient acquired the infection are described. The occurrence of tetanus after vaccination in a girl, aged 3 years, is reported. Eight days after the scarification the lesion was the customary pustule. It was severely scratched, and an ulcer with uneven edges and an offensive odor developed. The muscles of the face contracted, swallowing became difficult and finally the whole body became rigid. Tetanus antitoxin, 10 cc., was given intrathecally and 20 cc. subcutaneously; this was repeated the following day. On the third day there was no fever, but there was a rapid pulse rate, dyspnea, apnea and alarming cyanosis. Inhalations of oxygen and the subcutaneous injection of the gas were tried, but the child died. Cultures from the lesion yielded *Bacillus tetani*. Necropsy showed marked congestion of the meninges, passive congestion and infarcts in the lungs.

DWYER, Kansas City, Mo.

AFEBRILE TYPHOID. MARTINEZ VARGUS, Med. de los niños **31**:6 (Jan.) 1930.

Just as scarlet fever occurs without fever, so also does typhoid occur without fever. The author refers to a case in the literature of a youth, aged 17, who became ill with anorexia, headache and epistaxis, without elevation of temperature. Later there developed rose spots, meteorism and splenomegaly, but the temperature continued between 36.9 and 37.4 C. (98.4 and 99.3 F.). The blood culture was negative, the Widal test positive and the typhoid bacillus was isolated from the feces.

The author reports a case in a girl, aged 3 years, presenting the usual prodromal symptoms and a positive agglutination test. For forty-three days the temperature remained normal; just before death it rose to 40.8 C. (105.4 F.).

DWYER, Kansas City, Mo.

VACCINATION ENCEPHALITIS. A. ECKSTEIN, H. HERZBERG-KREMMER and K. HERZBERG, Deutsche med. Wchnschr. **56**:264, 1930.

Smallpox virus was found in the blood of eight children between the third and tenth days after vaccination with reaction, and absent from the blood of nine others. None of the spinal fluids obtained from children contained virus, even when the virus could be demonstrated in the blood. The spinal fluid of one of three infants with symptoms of encephalitis produced by the vaccine contained virus on the twelfth day.

BRESLICH, Chicago.

ENCEPHALITIS AFTER VACCINATION. BRUCKNER, Med. Klin. **26**:239 (Feb. 14) 1930.

Two cases of postvaccinal encephalitis are described, both occurring in children not older than 13 months. In one case there was complete healing; in the other case mental deficiency resulted from the acute process. The incubation period was six days in both cases.

ZENTAY, St. Louis.

Diphtheria Prophylaxis in Closed Institutions. B. Doll, Med. Klin. **26**:277 (Feb. 21) 1930.

In an orphans' home where a diphtheria epidemic started, the author employed Löwenstein's toxoid ointment method for prophylaxis. Three applications were made at an interval from fourteen to eighteen days. No additional cases appeared after the beginning of immunization. Schick tests will be made later to determine whether immunity actually developed in the children or not.

Zentay, St. Louis.

A Case of Hemiplegia After Diphtheria. Otto Saxl, Med. Klin. **26**:307 (Feb. 28) 1930.

Hemiplegia as a complication of diphtheria is not common. The author observed a case in a child, 8 years of age. The hemiplegia appeared in the third week after previous clinical symptoms of myocarditis. There was facial paresis, paresis of the twelfth nerve and a motor aphasia. There was a combination of central and peripheral paresis with secondary changes on the same side. The outcome was favorable with some impairment of function on the affected side.

Zentay, St. Louis.

Treatment for Diphtheria with Antitoxin. T. Brugsch and W. Grunke, Med. Klin. **26**:497 (April 4) 1930.

The virulence of diphtheria has increased in recent years. The authors studied 180 unselected patients in their hospital, treated during the previous two years. The total mortality was 23.9 per cent. This figure appears rather unfavorable for the antitoxin treatment for diphtheria, but if the date of the injection of antitoxin is considered, the picture immediately changes. In sixteen patients to whom antitoxin was given on the first day, there was 100 per cent recovery. The mortality increased to 18.5 per cent in patients to whom antitoxin was given on the second day, to 24.5 per cent in those given it on the third day and to 37.1 per cent in those given it on the fourth day. The conclusion in this study is that diphtheria antitoxin must be given on the first day if good results are to be hoped for.

Zentay, St. Louis.

Observations in a Measles Epidemic in a Refugee Camp. H. Gebhardt, Med. Klin. **26**:548 (April 11) 1930.

In a camp of German refugees coming from Russia, an epidemic of measles broke out which presented a severe picture. Altogether 208 cases were observed; 67 per cent of these showed some form of complications. The mortality was 23.7 per cent. The principal factor producing this high mortality seems to have been the unsatisfactory diet of these refugees, which was lacking in vitamins.

Zentay, St. Louis.

Results of Immunization with Löwenstein's Diphtheria Salve in the Midst of a Diphtheria Epidemic. Raimund Jahoda and Arthur Streit, Wien. klin. Wchnschr. **43**:300 (March 6) 1930.

Raimund Jahoda and Arthur Streit give the following conclusions concerning the use of Löwenstein's percutaneous diphtheria salve in the midst of an epidemic of diphtheria. The morbidity of diphtheria in the institution in which the salve was used was greatly reduced, while the epidemic continued in full force in the surrounding neighborhood. The salve was used without the slightest discomfort or injury to the children. The number of diphtheria carriers remained at 5 per cent, fifty-one days after the immunization. The authors conclude that immuniza-

tion with the percutaneous method is simple and harmless, and gives a favorable percentage of immunity. They recommend its use in thickly populated asylums for children and in the schools, both in ordinary times and in the midst of an epidemic of diphtheria.

A. F. ABT, Chicago.

ACTIVE IMMUNIZATION AGAINST DIPHTHERIA. FELIX BASCH, Wien. klin. Wchnschr. **43**:449 (April 10) 1930.

Felix Basch concludes that infrequently a negative phase can be produced in active immunization against diphtheria. It follows that whenever there is a possibility of direct exposure, active immunization should not be undertaken before passive immunity has been produced. Furthermore, persons giving a negative reaction to the Schick test should be immunized, because we may find only a very slight degree of immunity among them. In this way we may hope to cut down the number of immune diphtheria carriers. When passive and active immunity are undertaken simultaneously with the percutaneous salve method of Löwenstein, there is not the slightest unfavorable influence on the patient. The author expresses the opinion that every patient should be given the Shick test at some period after the immunization, and that if the reaction is still positive, a further immunization should be attempted.

A. F. ABT, Chicago.

EXPERIMENTAL INVESTIGATIONS OF POSTVACCINAL ENCEPHALITIS. J. P. HU and H. S. FRENKEL, Zentralbl. f. Bakteriol. (Abt. I) **112**:412, 1929.

The authors injected the neurovaccine of Gallardo into rabbits cutaneously and studied the effects. A large proportion of the animals died about the tenth day after inoculation. In these rabbits miliary foci of inflammation were found in various organs of ectodermal, mesodermal and entodermal origin. In the same organs the vaccine virus was recovered. The foci, especially in the lungs, are characterized by a marked proliferative reaction with a perivascular infiltration of mesenchymal cells and, in the opinion of the authors, are specific for the neurovaccine of Gallardo. The suggestion is made that the similar foci of inflammation in the brain in cases of encephalitis are caused by the vaccine virus or its toxins.

CANNON, Chicago.

Chronic Infections

DIMINUTION IN THE CIRCULATION OF THE SKIN A FACTOR IN DECREASING THE CUTANEOUS TUBERCULIN REACTION. J. D. PILCHER, Am. Rev. Tuberc. **21**:669 (May) 1930.

Well nourished tuberculous subjects react to comparatively small doses of tuberculin. Accompanying a decrease in weight as the infection progresses, there is a decrease in sensitivity to tuberculin, even to 10 mg. intracutaneously in extreme cases. This decrease in reactivity is considered to depend, in part at least on lessened circulation in the skin and subcutaneous tissues.

SMITH, Ogden, Utah.

"CLOSED" TUBERCULOSIS IN CHILDREN. VLADIMIR MIKULOWSKI, Am. Rev. Tuberc. **21**:686 (May) 1930.

In a child aged 3 years suffering from general cachexia due to tuberculous infection, a liquid, fetid diarrhea developed, and tubercle bacilli were demonstrated in the stools on two occasions. A diagnosis of tuberculous ulceration of the intestines was made. Autopsy showed rather extensive glandular tuberculosis, together with involvement of one phalanx of the middle finger of the right hand. There were no tuberculous changes in the pulmonary parenchyma or in the intestines. By animal inoculation, the feces and bile were found to contain tubercle

bacilli. This case confirms the observations of others that the tubercle bacilli found in the feces in cases of closed tuberculosis are of biliary origin. The presence of the bacilli in the bile is a result of a more or less severe bacteremia which may be present in cases of lymphatic or caseous tuberculosis. The finding of tubercle bacilli in the feces is therefore a valuable diagnostic sign of tuberculous infection in the absence of other bacteriologic or clinical evidence, especially since it has been shown that these are the only acid-fast bacilli found in the human intestinal contents.

SMITH, Ogden, Utah.

TUBERCULOUS MENINGITIS IN CHILDREN. HARRY S. SNYDERMAN, M. J. & Rec. **131**:508 (May 21) 1930.

Tuberculous meningitis is the most common form of leptomeningitis in children with the exception of epidemic outbreaks of the cerebrospinal form. It is rare under 6 months of age and is more frequent in the second year of life. Though gradually diminishing in degree a special tendency to this disease persists until the end of the sixth year. The author gives as the two chief causes of the infection: (1) living in close contact with other persons who are suffering from some form of tuberculosis, and (2) the prolonged use of unboiled milk. The typical form is usually divided into: (1) the stage of irritation, (2) the stage of pressure and (3) the stage of paralysis or coma. The insidiousness of the onset often makes the diagnosis difficult at first. The symptoms in the different stages are described in the paper. Lumbar puncture is the only means of making a positive diagnosis. Tuberculous meningitis is invariably fatal, no matter what treatment is employed.

WILLIAMSON, New Orleans.

EPITUBERCULOSIS. BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **23**:831 (April) 1930.

A case of epituberculosis was reported in a boy aged 3 years. The mother had current attacks of tuberculous pleurisy, one sister had suffered from tuberculous peritonitis, and three other children, the youngest 2 years of age, gave a positive reaction to the Mantoux test.

WILLIAMSON, New Orleans.

VACCINATION WITH B. C. G. H. LEMAIRE, Nourrisson **18**:95 (March) 1930.

This article constitutes a favorable report on vaccination with B. C. G. It is not denied that tuberculosis can sometimes invade the immunized patient, but when it does, it is practically always in one of the four benign forms: (*a*) that showing only a positive tuberculin reaction, (*b*) the larval type with polyadenopathy and with or without splenomegaly and disease of the hilus, (*c*) tracheobronchial adenopathy with pulmonary epituberculosis or (*d*) scrofula with one or more of its various manifestations. The appearance of a more severe type is a rare exception. In the author's experience the vaccination is innocuous and of itself has never been responsible for the development of a malignant or fatal tuberculous infection.

MCCLELLAND, Cleveland.

THE VALUE OF THE TUBERCULIN TEST IN DETERMINING THE EFFECT OF ANTITUBERCULOUS VACCINATION ACCORDING TO THE METHOD OF CALMETTE. A. WALLGREN, Rev. franç. de pédiat. **5**:739 (Dec.) 1929.

Wallgren discusses the question of the rapidity with which immunity is established following vaccination with B. C. G. When it is administered orally, considerable time probably elapses before immunity develops, certainly before allergy develops. He concludes that when the child is to be taken back into an infected environment, the parenteral method of vaccination with small doses is preferable. With this method, allergy appears at the end of six or eight weeks.

LESLIE, Evanston, Ill.

Syphilis of the Skeleton Other Than the Long Bones in Infancy. M. Péhu and A. Policard, Rev. franç. de pédiat. **6**:50, 1930.

This is the last of a series of excellent articles on changes in the bones in the syphilis of infancy. The changes in the skeleton other than the long bones is of little interest clinically. There is no definite symptomatology, and the lesions can be detected only by roentgenography, in which a special technic is necessary. The changes are less extensive; there is not the same amount of disorganization, and the osteochardritis, so pathognomonic when seen in the long bones, does not exist at all in the membranous bones and to only a slight extent in the vertebra, the pelvis and the shoulder girdle.

Leslie, Evanston, Ill.

Study of the Skin Reaction of Pirquet with Human and Bovine Tuberculin in the Tuberculosis of Children. B. Benvenuti, Riv. di clin. pediat. **28**:361 (May) 1930.

The author did parallel Pirquet tests with human and bovine tuberculin on 200 children; 94 children did not react with either tuberculin although 29 had clinical tuberculosis. Of the 106 children who showed a positive test, 35 reacted only to the human tuberculin, 21 only to the bovine tuberculin and 50 to both tuberculins. Of the 50 children reacting to both tests, 23 reacted with equal intensity to each tuberculin, 14 more strongly to the human and 13 more strongly to the bovine tuberculin.

The author concludes (1) that some cases of tuberculosis do not react even to bovine tuberculin and (2) that it is advisable to use both forms of tuberculin, especially when one suspects a surgical form of tuberculosis.

Hopkins, Boston.

The State of Antituberculous Vaccination. M. da Rocha, Jr., Arch. de pediat. **2**:162 (March) 1930.

The author reviews the French and German literature on antituberculous vaccination.

Sanford, Chicago.

A Line of Hypercalcification of the Metaphysis as a Typical Process of Congenital Syphilis. A. Izzo, Rev. chilena de pediat. **1**:69 (Feb.) 1930.

Izzo found that a line of hypercalcification of the metaphysis is characteristic of congenital syphilis. He always obtained a positive Wassermann reaction in cases showing this, even when other common indications of syphilitic bone were absent. He believes that this process is due to an area of repair, following a zone that has been destroyed.

Sanford, Chicago.

Studies on Children Coming from a Tuberculous Environment in the Out-Patient Department. G. O. Laves, A. Sandels and G. Weber, Monatschr. f. Kinderh. **46**:519 (April) 1930.

The writers report studies on 163 boys and 144 girls aged from infancy to 14 years, who came from tuberculous environments. They all gave positive Pirquet tests. The index of their condition was the roentgenogram. Due to the authors' inability to follow the cases, the study loses much force. Apparently, children coming from tuberculous environment with positive Pirquet reactions show more typical clinical and roentgen tuberculosis than those coming from a nontuberculous environment.

The authors concluded that from one roentgen examination and, in certain cases, one blood sedimentation test and even one clinical examination, the observer obtains little idea of the severity of the tuberculosis or the prognosis. They believe that one must study cases at frequent intervals in order to have any accurate conception of the nature of the pulmonary involvement.

Gerstley, Chicago.

THE MORPHOLOGIC DEVELOPMENT OF CHILDREN INFECTED WITH TUBERCULOSIS. L. SCHAPIRO, Ztschr. f. Kinderh. **48**:640, 1930.

Comparative observations on children infected with tuberculosis and those not infected showed the relation of physical development to a previous tuberculous infection. The body length of children in infancy as also in the periods of "storage," from 1 to 4 years and from 7 to 10 years, is greater in tuberculous children than in normal children of the same age. In the periods of growth in length, from 4 to 7 years and from 10 to 15 years, the conditions are just reversed. At such times the tuberculous children remain much behind the nontuberculous. The weight of tuberculous children is less at all ages, in boys as well as in girls, than the weight of noninfected children. In the periods of "storage" the absolute values of the circumference of the chest showed no remarkable deviation from the normal. In the periods of growth in length the circumference of the chest in tuberculous children is smaller than that in normal children of the same age.

EMERSON, Boston.

RESULTS OF B. C. G. INOCULATIONS IN AMSTERDAM. M. R. HEYNSIUS VAN DEN BERG, Ztschr. f. Tuberk. **55**:401, 1930.

The oral administration of B C G to two hundred and sixty infants showed that the procedure is harmless, according to an observation over four years. There does not seem to exist any parallelism between skin allergy and immunity. The tuberculosis mortality during the first two years of life in children who had a positive Pirquet reaction within the first year of life was 6.2 per cent in the inoculated group, as compared with 52.3 per cent in the noninoculated group.

MAX PISSER.

Internal Diseases

THE CARDIAC RESPONSE IN ACUTE DIFFUSE GLOMERULONEPHRITIS. I. JESSE LEVY, Am. Heart J. **5**:277 (Feb.) 1930.

Circulatory decompensation may suddenly appear in acute diffuse glomerulonephritis, and the recognition of its presence is extremely important in the diagnosis and treatment of the latter. The sudden advent of circulatory decompensation as evidenced by dilatation of the right side of the heart, pulmonary congestion and an enlarged and tender liver in the absence of valvular disease and lesions of the coronary arteries, should lead one to suspect the presence of acute nephritis.

Pulmonary edema may be the cause of death in acute nephritis. In addition to dietetic measures, cardiac supportive treatment is indicated, and the liberal use of caffeine products such as theocalcin, etc.

MANNING, Santa Barbara, Calif.

ELECTROCARDIOGRAPHIC CHANGES IN QUIESCENT RHEUMATIC DISEASES IN CHILDREN AND YOUNG ADULTS. M. J. SHAPIRO, Am. Heart J. **5**:504 (April) 1930.

Electrocardiographic tracings were taken in 119 children giving a history of rheumatic disease, but in the so-called quiescent group, and on fifty normal children. Changes in the former group were found during acute rheumatic fever, though their frequency was less. The most prevalent and characteristic change was the absence of the iso-electric period between the R or S wave and the T wave and the variability of this portion of the tracing.

MANNING, Santa Barbara, Calif.

CHANGES OCCURRING IN THE BLOOD OF THE NEW-BORN FOLLOWING ULTRAVIOLET THERAPY. H. N. SANFORD, Arch. Physical Therapy **11**:101 (March) 1930.

In fifty new-born infants, short exposure to ultraviolet light increased the bleeding time and the blood platelets. There was no effect on the coagulation time.

Short exposure to the ultraviolet light would therefore serve as a therapeutic measure in infants with delayed bleeding time, but their coagulation time would have to be decreased by other means.

Short exposure of 200 new-born infants to ultraviolet light increased the hemoglobin content and number of red cells to a slight extent in an average number of cases. In cases in which the hemoglobin content and number of red cells are lower than normal, the hemoglobin and cells are increased to a greater extent and tend to remain nearly normal.

Exposure of 120 new-born infants to ultraviolet light increased the total white count to a slight extent, the lymphocytes being increased at the expense of the polymorphonuclear leukocytes. The number of young or single-lobed nucleated cells of the polymorphonuclear cells was increased. The older or multilobed forms were decreased. There was a rapid return to normal.

AUTHOR'S SUMMARY.

HODGKIN'S DISEASE IN A CHILD. ELISE S. L'ESPERANCE, J. Immunol. **18**: 127, 1930.

Chicken inoculations of Hodgkin's material again resulted in typical avian tuberculosis, and reinoculation from this into other chickens caused a more extensive tuberculosis with marked involvement of bones. Cultures of material from a reinoculated chicken gave a pure growth of tubercle bacilli, culturally of avian type. Treated guinea-pigs inoculated with the original material developed extensive lymphatic tuberculosis and cultures on egg mediums showed many of the characteristics of a growth of avian tubercle bacilli. Subcutaneous inoculation of a rabbit with the original material caused no infection, as frequently happens with pure culture of avian tubercle bacilli.

AUTHOR'S SUMMARY.

DEVELOPMENTAL DISEASES OF BONES. SAMUEL W. BOORSTEIN, M. J. & Rec. **131**:77 (Jan. 15) 1930.

Under the heading of development diseases of bones, the author included Legg-Perthes' disease, Osgood-Schlatter's disease and Kochler's disease, which usually occur at times of maximum development of the epiphyses. The four views as to etiology are: (1) slight trauma or repeated strains, (2) local circulatory disturbance, (3) mild infection and (4) endocrine disturbance.

The chief symptoms are mild pain, with sometimes a slight limp, and perhaps swelling and tenderness. The diagnosis in most of the cases is made on the roentgenographic observations. Osgood-Schlatter's disease is often diagnosed as traumatic separation of the tubercle of the tibia. The prognosis in these conditions in general is good. The ultimate result in Legg-Perthes' disease is never a normal joint, but the function is fair; in that of Osgood-Schlatter's disease the result is perfect. The principle of treatment is to relieve the pull of the big muscles, and in coxa plana to relieve pressure on the deformed and softened head. The means used is immobilization in plaster or a brace during the acute stage, followed by massage and exercises.

WILLIAMSON, New Orleans.

THE RELATION OF ACETO-ACETIC ACID TO DIABETIC COMA AND THE CAUSE OF DEATH. E. C. DODDS and J. D. ROBERTSON, Lancet **1**:852 (April 19) 1930.

1. A study of (*a*) the aceto-acetic acid and (*b*) the alkali reserve content of the blood in patients in diabetic coma failed to support the theories of ketosis and acidosis, respectively, as a cause of this condition. Thus, in many cases patients with noncomatose diabetes were found to have higher aceto-acetic acid content than the comatose patients, and it was found impossible to correlate the blood analyses with the clinical condition of the patient.

2. On recovery from coma it was found that the aceto-acetic acid content rose, thereby further indicating that the enol theory of diabetic coma is improbable.

3. In the fatal cases it was found that death was preceded by a persistently falling blood pressure, and the importance of circulatory failure is indicated.

4. The occurrence of leukocytosis in coma is confirmed.

LANGMANN, New York.

A CASE OF CONGENITAL RHABDOMYOMA OF THE HEART. GEORGE BROWN and JOHN GRAY, Lancet **1**:915 (April 26) 1930.

A male infant, aged 3 months, died in a bout of crying brought on by a slight injury that he received. He had shown no edema, cyanosis, hemoptysis or ascites.

In two respects the structure described differs rather strikingly from the usual description of rhabdomyomas of the heart:

1. The structure is usually more myoblastic and less differentiated than that seen here. There is also a much more extensive vacuolation and an even greater cellularity.

2. The accompanying connective tissue seems to be more abundant in this instance than ordinarily.

LANGMANN, New York.

THE RELATION OF THE PARATHYROID GLANDS TO DISORDERS OF BONE. J. CLIFFORD HOYLE, Practitioner **124**:532 (May) 1930.

In 1915 an active extract of the parathyroid glands was prepared by Collip. Extensive experimentation by Bauer, Aub, Albright and other workers has demonstrated that injection of the extract causes decalcification of bone. This has been shown both roentgenographically and histologically. It is therefore believed that hyperactivity of the parathyroids may be a specific cause of decalcification.

The author states that experimental data suggest that the pathologic changes in bone found in osteomalacia may be due to deficiencies of diet, disorders of the endocrine glands or a combination of these factors. In these patients there is a negative calcium balance, a low amount of calcium in the blood and a deficiency in the calcium content of the bones. The disease is prone to affect adolescent girls and pregnant women. Erdheim was the first to point out the occurrence of enlargement of the parathyroids in osteomalacia. Other workers have confirmed his observation, and simple hypertrophy, hyperplasia and benign or malignant tumors of the parathyroids have been described.

In osteitis fibrosa, parathyroid enlargement has also often been noted. Frequently the increase in size is found to be due to a tumor mass, usually an adenoma. In these patients there is sometimes evidence of increase in activity of the parathyroids as shown by the persistant increase in the calcium content of the blood, a secondary increase in calcium excretion and a negative calcium balance. Removal of the adenomas has been followed by arrest of the lesions and later by normal observations on blood calcium.

Parathyroid extract-Collip has been found to aid in healing of delayed union of fractures. The writer refers to Hulper's experimental work on cats in which injections of the extract were used. It was found that by using the extract the degree of calcification increased from 20 to 35 per cent as compared with controls.

In the treatment of chronic plumbism, Hunter and Aub showed that an average daily dose of 55 units of parathyroid extract-Collip raised the excretion of lead from an average of 1 to 2 mg. to as much as 6 to 10 mg. for a three day period. The excretion of lead and calcium followed an approximately parallel course, and in both cases excretion persisted for about a week after the treatment was discontinued.

Hypoparathyroidism, although usually due to accidental surgery, sometimes occurs spontaneously. It is characterized by (*a*) liability to acute tetany, especially during pregnancy or lactation (*b*) the occurrence of cataract and (*c*) defective deposition of calcium in the teeth during the period of growth.

SAPPINGTON, San Francisco.

PERSISTENT PNEUMOTHORAX. H. H. C. GREGORY, Proc. Roy. Soc. Med. **22**: 117 (Dec.) 1929.

A case of persistent pneumothorax was reported in an infant, aged 8 months, who was admitted to the hospital on account of pigeon breast and dyspnea. On physical examination, respirations were found to be rapid, there was a hyperresonant note over the whole left side, and breath sounds were absent. The heart was felt and heard to the right of the sternum. Roentgenograms revealed a left pneumothorax with no signs of the left lung. The right side was occupied by a lung with many patchy shadows, and on withdrawing air from the pleural cavity above the shadow, the heart was seen a little to the left of the sternum under the screen; by the time the plate was taken three minutes later, however, the shadow had disappeared and the cavity was again full of air. The persistent pneumothorax was obviously kept up by a bronchial fistula which was present at or soon after birth. There was no clue to the cause of the fistula; it may have been congenital.

WILLIAMSON, New Orleans.

FAMILIAL ACHOLURIC JAUNDICE (SON, MOTHER AND GRANDMOTHER). H. V. MORLOCK, Proc. Roy. Soc. Med. **23**: 430 (Feb.) 1930.

A case of acholuric jaundice was reported in a boy, aged 8 years. On admission to the hospital his only complaint was pain in the left side of the abdomen. The conjunctivae were jaundiced and the spleen was enlarged. The results of an examination of the blood is given in full. The mother had suffered from the disease for fourteen years but refused splenectomy. The grandmother had been known to have had the disease for thirty years. The spleen was greatly enlarged. The grandmother's brother also suffered from the same condition; he died at the age of 36.

WILLIAMSON, New Orleans.

ENDOCARDITIC FORM OF STILL'S DISEASE. R. DEBRÉ, R. BROCA and M. LAMY, Arch. de méd. d. enf. **33**:212 (April) 1930.

Still's disease is rarely seen in France; the first discussion of this recognized clinical entity was published by Rohmer in 1922, and the second thesis appears at this time.

The pathognomonic signs of Still's disease—arthritis, adenopathy and hypertrophy of the spleen—may be accompanied in rare instances by pericarditis, but in Still's original monograph he insists that endocarditis is never a feature of this disorder. The authors quote cases of Parkes-Weber and of Poynton in which lesions of the endocardium were present, and they report an interesting one of their own in a boy, aged 12. There was great hypertrophy, with both mitral and aortic insufficiency, developing several years after the original invasion of polyarthritis and progressing rapidly to the usual fatal termination.

AMESSE, Denver.

FOREIGN BODIES IN THE DIGESTIVE TRACT OF THE INFANT. PETIT DE LA VILLÉON, Bull. et mém. Soc. de chir. de Paris **22**:231 (March 21) 1930.

The author emphasizes his belief in watchful waiting in the case of infants who have swallowed foreign bodies, calling attention to the dangers attending abdominal operations in the very young. Spontaneous elimination is the rule, in his experience.

BIEKER, St. Petersburg, Fla.

INTESTINAL SPIROCHETES IN DIARRHEA IN INFANTS. TRIAS MAXENCHS, Bull. de la Soc. Catalana de pediat. **1**:9 (Jan.) 1928.

After reviewing the literature, the author reports five cases in which spirochetes were found. He deduces from the cases studied that (1) the presence of

spirochetes in the feces coincides with grave digestive disorders in the child, (2) the spirochetes must be sought in the mucus portions of the stool, (3) the diluting of the material in water or broth is sufficient at times to destroy them and to give a negative result, (4) the intestinal flora is not modified with the appearance of spirochetes and (5) the increase of spirochetes in the feces coincides with the time of fever.

WATSON, Chicago.

TREATMENT FOR ANOREXIA. AURELIO RAFAEL POZAS, Med. de los niños **31**: 11 (Jan.) 1930.

The various causes of anorexia are discussed, and particularly the mental aspect of the condition. In the infant that refuses milk the common causes should be sought, such as anemia, syphilis, disturbances in dentition and tuberculosis. When none of these is present, it is advisable to isolate the child and use lavage with Vichy water to rid the stomach of offensive mucus which may be the reason for the loss of appetite.

DWYER, Kansas City, Mo.

THERAPY OF PYLOROSPASM. EMILIE SCHROEDER, Fortschr. d. Med. **48**:93, 135, 177, 1930.

Physical therapy for pylorospasm includes the following: warm lead fomentations, diathermy and high frequency electrical treatment, all of which have their fervent advocates. Surgical therapy includes jejunostomy, resection of the pylorus, gastro-enterostomy and stretching of the pylorus. In 1910, Weber described partial pyloroplasty in which a longitudinal section through the serous and muscular coats is made and united by cross suture; the name given to the operation was submucous pyloroplasty. Under Rammstedt it became very popular. This was followed by a considerable division of opinion as to when operative measures should be adopted. A pyloric tumor is rather infrequently palpable in these cases, and Konrad and Kielmann described cases of congenital pyloric hypertrophy without clinical symptoms. Modern pediatrics finds no clear distinction between purely spastic and hypertrophic stenosis of the pylorus, and the consensus is in favor of operating only in the severer cases. Strauss, Leall and Heile recommend surgical intervention in cases in which from 70 to 80 per cent of the bismuth ingested remains in the stomach after four hours, but roentgenograms do not always give the correct estimation of the seriousness of the condition. According to Bloch, a rapid decline of weight is a vital indication for operation. To allow the condition to persist for a long time is apt to lower the child's resistance to various infections in the opinion of Finkelstein. Hildebrandt and Strauss have preferred other operative measures as improvements on the Rammstedt operation. The great danger after the operation is vomiting and perforation peritonitis. Kirschner uses chloroform narcosis. Others use ether and even local anesthesia. Eckstein and Romminger used methylpropylcarbinolethyl carbonate with the best results.

Ibrahim, in 1913, compiled the mortality rate from purely corrective treatment as 10.2 per cent in 400 cases, as contrasted with 10.6 per cent of 597 cases from operative methods.

HART, Greenwich, Conn.

TREATMENT FOR HYPOCHROMIC ANEMIAS WITH LARGE DOSES OF IRON. HANS SCHULTEN, München. med. Wchnschr. **77**:355 (Feb. 28) 1930.

The success of liver therapy in pernicious anemia has aroused new interest in the use of iron in other types of anemia. In extensive losses of blood from hemorrhage, spontaneous recovery usually takes place. If this does not occur in three or four weeks some stimulus to blood regeneration should be used. Iron is now considered of little benefit. However, Schulten thinks that even though the amount of iron utilized by the patient is very small, large doses of reduced iron

should be given. Reduced iron is not chemically pure and other minerals, such as nickel or copper, may act synergistically with the iron. The author has given as much as 6 Gm., and in one case 10 Gm., of reduced iron daily with good results.

BRAHDY, Mount Vernon, N. Y.

THE TREATMENT FOR GONORRHEAL VULVOVAGINITIS. A. NOHLEN, Münchn. med. Wchnschr. **77**:362 (Feb. 28) 1930.

Nohlen reports a treatment for vulvovaginitis which he has found better than any of the other seventeen methods used in about 250 children in the Children's Hospital in Düsseldorf. He uses a modification of the apparatus and technic originally described by Hübner and Stolzenberg. A glass irrigating nozzle which fits watertight over the vulva is used. The vagina is irrigated under pressure with silver nitrate solution (1:4000) for half an hour every other day. This is preceded and followed by irrigation for ten minutes with diluted potassium permanganate. A soap sitz-bath is given daily. The children are active but are kept in the hospital. If vaginal smears are negative after three or four weeks, the patients go home and report in about a month for follow-up examination. Fifteen children have been successfully treated. The longest period of treatment necessary was fifty-five days; the average was twenty-seven days.

BRAHDY, Mount Vernon, N. Y.

A CURED CASE OF APLASTIC ANEMIA. BIRK, Münchn. med. Wchnschr. **77**: 575 (April 4) 1930.

Birk reports successful treatment in a case of aplastic anemia. The anemia was noted when the patient was 1 year of age. There was nothing unusual in the past history. The feeding had been properly supervised. Physical examination gave negative results except for the severe anemia and a mild nasopharyngitis. The liver, spleen and lymph nodes were not enlarged. The red cell count was 980,000 and the hemoglobin 16 per cent. In order to rest the bone-marrow, Birk decided to give repeated transfusions in addition to other forms of therapy, such as iron and arsenic by mouth and a diet including raw vegetables, liver fruit juices and bone-marrow. Most of the forty transfusions were given into the longitudinal sinus, but some were intraperitoneal or intramuscular. During the first month that transfusions were given at short intervals (from three to five days) the child improved. Following this no transfusions were given for three weeks, resulting in a rapid decrease in hemoglobin and red cells. Immediate improvement followed the reinstitution of frequent transfusions. Ten months after admission the child was discharged with 4.8 million red cells and 84 per cent hemoglobin. Examination two months later showed 5.2 million red cells and 79 per cent hemoglobin.

BRAHDY, Mount Vernon, N. Y.

OSTEOGENESIS IMPERFECTA AND ENDOCRINE SYSTEM. ERIK JOHANNES KRAUS, Virchows Arch. f. path. Anat. **274**:37, 1929.

In two instances of osteogenesis imperfecta no signs of premature development of the endocrine glands could be found.

PLAUT, New York.

THE PHOSPHATIDE AND CEREBROSIDE CONTENTS OF THE SPLEEN AND LIVER IN GAUCHER'S DISEASE OF CHILDREN, IN NIEMANN-PICK'S DISEASE, AND NORMALLY. EMIL EPSTEIN, Virchows Arch. f. path. Anat. **274**:294, 1929.

The figures for lecithin as given in the literature are far too high. If one extracts normal spleens with ether, working with fresh material and with formaldehyde-fixed material, the residue after evaporation of the ether is three times as heavy in the fresh material as in the fixed. It is different after extraction with

alcohol; generally the fresh spleen leaves a residue which is only one-tenth heavier. Therefore, organs for lipoid extraction must be kept unfixed on ice, and, if possible, given to the chemist the same day. One can keep the organs for some time by slicing them and rubbing chemically pure sodium chloride into the slices.

PLAUT, New York.

NIEMANN-PICK DISEASE (LIPOIDOCELLULAR SPLENOMEGALY). H. SMETANA, Virchows Arch. f. path. Anat. **274**:697, 1930.

In a first-born Jewish girl, enlargement of the liver was noted at age of 4 months together with increasing brownish discoloration of skin. The blood was normal. At the age of 20 months, the child could not sit and was unable to support her head. She was idiotic, but not blind. The spleen was much enlarged. Death occurred from pneumonia. Autopsy showed soft, edematous meninges, a firm brain, with thick convolutions somewhat similar to a brain in familiar amaurotic idiocy; a firm spleen (*222* Gm.), reddish-white pulp; yellowish intestinal mucosa and mesenteric lymph nodes; reddish-yellow marrow of the femur, and a firm, yellowish-gray liver (1,140 Gm.).

Large, vacuolized cells from 20 to 60 microns in diameter were found in all the organs, most of them having one nucleus. They were numerous in the spleen, liver, lung, thymus, lymph nodes and brain. With sudan III stain, all colors from light yellow to brown red were found. With the Smith-Dietrich stain, gray to black granules were found in all the cells. Doubly refractive material was present in large amount in the thymus, bone-marrow and lymph nodes, and small amounts in the ovaries, intima of the aorta and perivascular tissue in the brain. The liver and spleen contained no doubly refractive material. In the liver, the large cells protruded into the capillaries, endothelial cells separating them from the liver cells. All transitions from normal Kupffer cells, containing a few vacuoles, to the large, completely vacuolized cells, were traced. In the lungs the large cells contained up to twenty nuclei and occasionally large fat droplets. It is possible that large amounts of the lipoid material resulting from the breaking down of the large cells in all the organs, were carried into the lung and thus were responsible for the different appearance of the large cells in the lungs.

Chemical examination of fresh liver, spleen and brain showed much increase in lecithin and phosphorus-containing lipoids. No kerasin could be found. The chemical examination is the best means of differentiating between Gaucher's disease in infants and Niemann-Pick's disease. For the Smith-Dietrich stain the author recommends mordanting and staining in bulk, followed by celloidin embedding and differentiation under the control of the microscope.

PLAUT, New York.

METABOLISM STUDY IN THYROID AND PANCREATIC DISEASE IN CHILDREN. EDMUND NOBEL, Wien. klin. Wchnschr. **43**:333 (March 13) 1930.

Edmund Nobel points out in this article the increasing use of metabolic studies in hypothyroid conditions in children. He brings out the fact that metabolic studies in these children are difficult to evaluate because of the lack of standard metabolic values for normal children. The abnormal body proportions of myxedematous children make it even more difficult to compare the values with the inadequate standards which we now possess. The author also points out the difference in the dosages of prepared thyroid substances.

In discussing pancreatic insufficiency he gives as an example so-called intestinal infantilism or celiac disease. Pancreatic preparations, in the form of pancreatin, did not give satisfactory therapeutic results in this condition. The author believes that a full mixed diet, as recommended by Shick and Wagner, will help to heal the injured endocrine glands and lead to recovery in this condition.

A. F. ABT, Chicago.

THE TREATMENT FOR BRONCHIECTASIS IN CHILDREN. FELIX BASCH, Wien. klin. Wchnschr. **43**:301 (March 20) 1930.

Felix Basch, in discussing the treatment for bronchiectasis in children, recommends the use of emetin in combination with a transpulmin and a brand of arsphenamine. In one case of bilateral bronchiectasis, no therapeutic result was obtained with this combination of drugs, while pneumothorax of alternating sides produced healing. The author points out that in cases of chronic cough with slight expectoration following measles, whooping cough or grip, emetin in combination with other drugs should produce good results.

A. F. ABT, Chicago.

DIABETES MELLITUS IN CHILDREN. RICHARD WAGNER, Wien. klin. Wchnschr. **43**:402 (March 27) 1930.

Richard Wagner raises the theoretical question as to the possible congenital transmission of diabetes mellitus. He suggests the following methods of answering this question: (1) investigation of juvenile diabetes as to simultaneous occurrence of degeneration, (2) study of the inheritance of the disease, (3) biometric studies concerning the appearance of the manifestations of the disease, (4) division of diabetes among the races and (5) demonstration of the possibility of diabetes in identical twins.

A. F. ABT, Chicago.

Nervous Diseases

CISTERNA MAGNA PRESSURE SYNDROME. MARK S. REUBEN and JULIUS CHASNOFF, Arch. Pediat. **47**:201 (April) 1930.

The writer calls attention to a syndrome (rapid pulse, rapid respiration, high or low temperature, occasional delirium) which may develop during the course of acute meningococcic meningitis. He feels that this group of symptoms is probably due to pressure on the medulla and possibly to distended cisternae. He has found that when these symptoms persisted as long as seven days, death invariably occurred. Marked improvement was noted following cisterna puncture. At the first tap, no serum is introduced, regardless of the character of the spinal fluid. If there should be a return of the symptoms, another tap should be performed, and if fluid withdrawn is turbid and if previous examinations revealed organisms, serum should be introduced, but no more than half the amount of fluid that has been withdrawn. It is advised that this procedure be carried out even if fluid can be obtained by lumbar puncture, since it is believed that the cisterna is not in communication with the rest of the subarachnoid space.

Case reports are included, also a description of the anatomy of the cisternae.

WADDELL, University, Va.

ACUTE ANTERIOR POLIOMYELITIS AT VEGA BAJA, PORTO RICO. E. GARRIDO MORALES, J. Infect. Dis. **46**:31, 1930.

Reports of epidemic poliomyelitis in the tropics are rare. Poliomyelitis has probably existed in endemic form in Porto Rico for some time; it has not been recognized or, at least, the cases and deaths have not been reported as such. No epidemic of the disease has ever been reported in Porto Rico before 1928. Poliomyelitis appeared in epidemic form (ten cases, one death) in the town of Vega Baja during April, May and June, 1928. The evidence strongly suggests that indirect personal contact played a major part in the spread of the disease. Apparently, the virus responsible for the present outbreak was not introduced from outside, but from a local source, presumably represented by cases which had occurred two years before in Vega Baja.

AUTHOR'S SUMMARY.

Spasmodic Head Retraction Following Encephalitis Lethargica. T. R. Hill and C. Worster-Drought, Proc. Roy. Soc. Med. **23**:270 (Jan.) 1930.

In 1924, a patient had an attack of epidemic encephalitis (lethargica) after which he became inattentive at school and suffered from nocturnal restlessness and noisiness. In 1927 there was a gradual onset of spasmodic movements of the head and face. The patient came under observation in 1928, at the age of 15; he then suffered from sudden muscular spasms, repeated frequently, during which the head was extended backward, the mouth was opened and the left side of face contracted as in smiling. The duration of the spasm was not more than a few seconds. The spasms could be controlled fairly well for a time and were best elicited when the patient walked up and down.

Williamson, New Orleans.

The Treatment of Chorea with Phenobarbital and Magnesium Sulphate: Considerations on the Physiopathology of Chorea. G. Marinesco, O. Sager and G. T. Dimitrescotti, Ann. de méd **27**:237 (March) 1930.

The authors report five cases of Sydenham's chorea which reacted favorably to subarachnoidal injections of magnesium sulphate within from five to six day intervals (0.008 mg. per kilogram of body weight in 25 per cent solution). Another therapeutic attempt was the subcutaneous injection of phenobarbital, 0.22 cg. of sodium phenobarbital dissolved in 1 cc. of distilled water. The injections were repeated every other day for from twenty to twenty-five days. A discussion of the etiology of chorea is added, based on the theories of Minkowski, Foerster, Wilson and others.

Weil, Chicago.

Anatomy and Pathologic Physiology of Sydenham's Chorea. J. Lhermitte and P. Pagniez, Encéphale **25**:24 (Jan.) 1930.

A review of the literature shows that a variable pathologic base is described in chorea. In 1920, Mery and Babonneix reported an observation of extensive pathologic changes of the cerebral cortex and of the basal ganglia, consisting of vascular infiltrations and cellular degenerations. In 1921, Henri Claude published observations of distention of the vascular sheaths, without infiltration, and of cellular degeneration in the basal ganglia. Delcourt and Sand reported a case with maximum involvement of the basal region, becoming lessened as one approached the cortex, bulb and cerebellum. Tinel, in 1914, had reported similar disturbances in the ganglia and in the frontorolandic area. Marie and Tretiakoff, in 1920, published ammounts of marked vasodilatation and infiltration of the adventitial sheaths with mononuclear cells, lymphocytes, plasmacytes and myelophages, both in the cortex and in basal regions. They also discovered inflammatory reactions of the locus niger. Similar studies were made by Harvier and Levaditi; also by Harvier and Decour in a man, aged 86, who succumbed to acute chorea and showed at autopsy vascular thrombosis with perivascular infiltration in the cortex. Slauk found intense lesions of the caudate, the thalamus, nucleus ruber, corpus Luysii and the perisylvian region. These were agglomerations of neuroglia.

Then follows a report of the case of a woman, aged 19, whose illness commenced early in November and progressed as a typical chorea to death in December. Grossly, there was evident congestion of the meninges. Microscopically, the examination was made in a most detailed way and yielded results which are summarized as follows: vasodilatation, vascular ruptures with capillary hemorrhage, distention of the adventitial sheaths by an albuminous exudation and cellular changes—tigrolysis and karyolysis, with the gradual reduction of the cytoplasm and the final destruction of the cell. As to topography, the lesions were predominant in the dentate nucleus, putamen-caudate segment of the striate body, and the Purkinje cells of the cerebellar cortex. On the basis of these, and similar reports, they believe that it is reasonable to think of acute chorea as divisible into two groups,

one characterized by more or less diffuse encephalitic lesions, and the other of a more degenerative type with vascular modifications.

The authors agree with Kinnier Wilson and others of the Hughlings Jackson school that destruction of a region of the central nervous system cannot account for positive phenomena such as spasms, contractures and choreo-athetotic movements; that all it can explain are phenomena of deficit. They accept, too, the idea of "diaschisis," in a general and dynamic way, whereby a lesion at one point may arouse inhibitions, or leases therefrom, in centers at a distance. But when it comes to agreement with the idea, seemingly experimentally substantiated, that chorea is due to direct pathologic change of the motor cortex, they object that the cessation of choreic movement in hemiplegia really proves nothing except that in hypertonic states such movements are impossible. They do concur, however, in the idea that it is impossible to conceive of choreic movements without the existence of a cortex. This is shown by the absence of anything simulating choreic movements in decerebrate rigidity; also by the generally accepted view that such movements cease during sleep and hypnosis. An hypothesis is ventured that the muscular disorder is influenced by disturbance of the cerebellothalamic tract.

ANDERSON, Los Angeles.

DISTURBANCES OF SLEEP IN SCHOOL CHILDREN. JEAN BÉNCH, Med. de los niños **31**:19 (Jan.) 1930.

Fatigue is a frequent cause of disturbance of sleep. In order to prevent this, a more equal allotment of the time devoted to work and to play is advised. Arsenic, phosphorus and strychnine as a tonic often gives good results. A preparation of morphine and barbital is recommended for intractable patients.

DWYER, Kansas City, Mo.

A CLINICOPATHOLOGIC STUDY OF DISEASE OF THE BRAIN IN EARLY CHILDHOOD WITH A PREDILECTION FOR THE STRIATAL SYSTEM. E. FÜNFGELD, J. f. Psychol. u. Neurol. **40**:85 (Dec.) 1929.

The patient whose case is reported was born in 1901; labor was difficult and development retarded; he did not walk until the age of 1½ years. Although he apparently carried out commands, recognized persons and objects, and was very playful, he learned to speak only a few words. At the age of 5 months he began to have epileptiform seizures which appeared at first daily but later every few weeks. At the age of 15 years he gradually developed a tremor of all four extremities with psychic changes characterized by increasing irritability and loss of interest. At the age of 22, the limbs became progressively rigid so that at 24 he was unable to get about at all; his general condition became markedly deteriorated.

On admission to the clinic he showed: expressionless facies, no tendency to spontaneous motility and periodic stereotyped jerking of the upper lip. Only the simplest commands could be executed; general asthenia with rigidity of the muscles of the neck and of the upper extremities was noted more marked in the proximal portions of the arm. There was slight tremor in the muscles of the shoulders and increasing in severity distalward and on intention. Rigidity was more marked in the lower limbs, especially on the right side; the right big toe was in dorsal flexion; the patient could walk only with assistance and then the body would be bent forward, very small steps would be taken, and the trunk and head held in flexion and to the right. There was loss of normal associated movements; occasional tendency to propulsion and facial grimacing and complete mutism. The pupils reacted to light promptly but not in convergence; ocular movements could not be tested. There were present right sided facial weakness; very lively arm reflexes; markedly diminished hand grip and abdominal reflexes; very lively knee jerks, with occasional ankle clonus and no Babinski sign. While testing for sensation, the arms and legs would develop a very coarse tremor; this would also occur during passive motion of the limbs.

Course.—During the patient's stay at the clinic no convulsions were observed. The neurologic status remained unchanged but the general condition became gradually worse and the patient died early in February, 1926.

Necropsy.—Except for the pallidum, which appeared perhaps darker than normal, the brain showed nothing abnormal macroscopically. The cerebral vessels were thin. The brain weighed 1,350 Gm. The other noteworthy necropsy observations were: tuberculous pleurisy, fibroid phthisis, a small heart, cloudy swelling of the parenchymatous organs and fatty degeneration and infiltration of the liver.

Microscopic Examination of the Brain.—Nissl Stain: The cerebral cortex was somewhat richer in glia nuclei than normal; this applied to all layers of the cortex structure of which, except for occasional shrinkage of the pyramidal cells in the third and fifth layers, was normal. The ganglion and glia cells contained an unusually large amount of fat. The vessel walls were in some areas somewhat thickened with collections of cells unusually rich in nuclei; the cells of the adventitial coat contained moderate amounts of lipoid. The pia was intact. The Betz cells were well preserved.

Myelin Fiber Preparations (Spielmeyer-Kulschitzki-Pal): In all fields examined (10, 8, 9, 4, 1, 2, 3, 20, 21, 22, 41, 42, 37, 5, 7, 39, 17, 18, 19) there were a definite diminution in the ground fiber network, especially in the deeper layers, whereas in the more superficial layers there was an abnormal discoloration of the myelin sheaths particularly the delicate fibers in the fourth layer. Although with the Bielschowsky stain, the axis cylinder network was well preserved, there was a slight but definite fibrous gliosis with glial fibers extending down the fourth and beginning to invade the fifth layers. Except for a diminution of the ground fiber network in Ammon's horn, this structure appeared normal.

The ganglion cells in the caudatum and putamen contained considerable quantities of lipoid; otherwise they were normal. There was, however, in these two ganglia a definite increase in glia nuclei. The thalamus was small and the ganglion cells and glia nuclei were strikingly dense, especially in the upper lateral and median nuclei. The fornix and anterior commissure appeared narrower than normal and were very rich in glia nuclei.

The pallidum also contained an unsually large number of glia cells. In its ventral third and, to a lesser extent, in the part adjacent to the putamen there were large quantitives of deposits symmetrically situated on the two sides; these deposits were of four varieties: 1, small, deeply stained ball-shaped masses some of which surrounded the vessels and others were situated diffusely in the depths of the tissue. As far as one can determine from the different staining reactions they represented precipitates of the tissue fluids. 2, Pigments, which with the Nissl stain appeared partly homogeneous and partly metachromatic; they were situated in the vessel walls and in the glia, and yielded the iron reaction. The quantity of this pigment was relatively slight. 3, the walls of many large veins were impregnated with "pseudocalcium" which stains red with thionin and also gives the iron reaction. 4, lipoid material which could be seen in fairly large amounts in the vessel walls as well as in the glia.

The ganglion cells of the pallidum were generally free from involvement except that here and there one could see rests of destroyed cells which appeared as small, dark stained structures with ill defined nuclei. Aside from the previously described deposits, there was no visible increase in the iron content of the tissues.

The appearance of the myelin fibers with myelin sheath stains was practically the same in the caudatum, putamen and pallidum as in the cortex. There was a definite reduction of the axis cylinders in the pallidum, and also a slight increase in fibrous glia in the striatum.

In the myelin sheath preparations the thalamus appeared poor in myelin; the delicate fibers in the upper lateral nuclear regions and in the ventral nucleus were poorly stained, although they did not seem to be diminished in number; on the other hand, there was unquestionably a loss of these delicate nerve fibers in the

median nucleus up to the pulvinary and especially in the ventral portions. In the Bielschowsky preparations the thalamus appeared normal, though there was probably a diminution of fibers in some areas between the thalamus and pallidum.

The ansa lenticularis was poorly stained but there did not seem to be an actual diminution of the fibers. The H 2 bundle was abnormally thin but the H 1 appeared normal. The corpus Luysii was intact.

In the mamillary body, as well as in the central gray, there was considerable decolorization of the fine delicate myelin fibers although it is difficult to say whether their number was diminished. The fornix and anterior commissure were almost entirely decolorized; this area was definitely smaller and also showed a fibrous gliosis.

The substantia nigra showed a remarkable lack of melanin in its ganglion cells which appeared smaller than normal, although they were not diminished in number and were overloaded with lipoid material. The cells in the reticular zone were intact but the glia in this region showed an enormous amount of lipofuscin. The entire substantia nigra was poor in delicate nerve fibers but the coarse fibers were well preserved. The lateral portion of the tegmentum was definitely smaller and showed a diminution in the number of fibers, but the medical portion did not take the stain well although it could not be definitely stated whether the fibers were diminished in number, nor could it be determined whether there was an actual increase of glia or a definite diminution in the fibrils.

The red nucleus, geniculate bodies, peduncles, corpora quadrigemina and medulla showed no definite pathologic changes, although here and there (central portion of the fibrous capsule of the red nucleus and in the medulla) the myelin fibers did not take the stain very well.

The dentate nucleus is intact, as is the entire cerebellum.

Comment.—The clinical picture in this case can be well correlated with the anatomic observations. The congenital mental defect would seem to be due to the definite diminution of the myelin fibers within the cortex. The disturbances in motility are due to pallidal involvement. It is difficult to determine how much of these disturbances is due to involvement of the substantia nigra, although it is noteworthy that the pallidothalamic fibers are less reduced in number whereas the pallidonigral tracts are much more involved in the pathologic process. Finally, the hyperkinetic phenomena could be attributed to the diminution of the striopallidal fibers which connect the pallidum with the large cells in the striatum, and to the involvement of the striatal fibers themselves.

In contrast to the cases described by O. Fischer, the histologic preparations in this case show nowhere any indication of destruction of the parenchyma of the nerve. The lipoid content in this case does not differ from that usually observed in the case of any person who has succumbed to a chronic infection. The deposits found in the various structures can be indicative only of metabolic changes of a chronic pathologic disorder and cannot be regarded as evidences of a necrobiosis. It may, however, be possible that the definite lack of melanin in the compact zone of the substantia nigra is of some pathogenetic significance. It is well known that in the new-born child the compact zone contains no melanin, and that it is not until the fourth year of life that this pigment gradually begins to develop. In view of this, one is unquestionably dealing in this case with an inhibition of melanin development which, according to the Vogts, may also be the basis for an inhibition of myelinization. Against this theory of failure of myemilinization in this case, however, is the clinical fact that the disorders of motility did not appear until the patient had reached his fifteenth year, although there would seem to be no difficulty in attributing the seizures which began in the fifth month of life and the mental defect which was also noticed very early in life, to defective myelogeny of the cortex. The next question then is, why did the motor disturbances first appear so late? According to Kaes, myelinization of the cerebral cortex, especially of the principal external layer (3), is not complete until well after the thirtieth year of life. One may also readily conceive that in the brain stem too some fibers do not become completely myelinated till after the termination of the second

decade of life. Finally, the pathologic changes in the case under discussion would seem to point to a disturbance of the "internal structure" of the basal ganglia and especially of the pallidofugal fibers. The author believes that it cannot be definitely excluded that myelinization of the basal ganglia ran its normal course during the early years of life, but, as in the cortex, it became inhibited during later development. He also has no doubt that the pathologic process in this case is closely related to that described by the Vogts as status dysmyelinatus, and that the inability of the tissues to take up the various stains represents merely a slight degree of this condition.

KESCHNER, New York.

PURULENT ASEPTIC MENINGITIS. H. KAUFBERSZ-MARYSOWSKA, Ztschr. f. Kinderh. **48**:120, 1929.

A baby, aged 5 months, had recovered from chickenpox one week before, when he came down with clear symptoms of meningitis. The spinal fluid showed 7,400 cells, 96 per cent of which were leukocytes, in as good condition as they were in the blood, which was of importance. Only one dose of serum was given. The child recovered and was in good health when last seen. The author considered the occurrence of chickenpox as a possible cause but was not satisfied that it was adequate.

EMERSON, Boston.

THE CONDITIONED REFLEXES IN CHILDREN WITH DECREASED RESPONSES TO STIMULI AND DIMINISHED INHIBITORY REACTIONS. A. WOLOWIR, Med.-Biol. J. (Moscow) **5**:110, 1929.

The work of Pavlov has shown that strong stimuli cause strong responses as well as strong inhibitory reactions. The disturbances in the delicate balance of the two have been described previously. In children with a predominant inhibitory mechanism, one gets hysterical manifestations, while children with dominant stimulatory responses develop reactions similar to those found in epidemic encephalitis. Children have been found who react very inadequately to very strong stimuli. Such a child was used as the subject in this experiment. He has been a patient in Krasnogorski's Clinic for several years, and was a dull, restless youngster, who previously had had a tuberculous infection of the bones with some sequelae.

In using the standard technic for elicitation of the conditioned reflexes, it was found that this child had a fundamental weakness in the development of responses to strong stimuli and also a weakness in the formation of inhibitions. The stimulus in this case was cranberries, accompanied with the sounds of a metronome and an electric bell.

The author comes to the conclusion that the weakness in responses, as well as the formation of inhibitions, points to a fundamental weakness of the cortical processes. A weak cortex does not provide sufficient regulatory influence over processes arising in the lower centers. Special technic can increase the inhibitory reaction. The asthenic type of salivary glands shows in hyposecretion, which is not increased by administration of drugs such as pilocarpine.

KASANIN, Boston.

Miscellaneous

FETAL DYSTOCIA DUE TO METASTATIC NEUROBLASTOMA OF THE LIVER. H. T. HAGSTROM, Am. J. Obst. & Gynec. **19**:672 (May) 1930.

Dystocia arose from an enlarged liver, which was found to weigh 700 Gm. The enlargement was due to metastases from a neurocytoma of the right suprarenal gland. The primary tumor of the suprarenal gland measured 6 by 6 by 5 cm. Delivery could not be completed except by partial evisceration of the tumor.

The pathologist reported congenital sympathicoblastoma of the right suprarenal gland, therefore of the Pepper type. Similar tumors of the left suprarenal gland usually metastasize to the ribs and cranium and are called the Hutchinson type.

ALLEN, Chicago.

GANGLIONEUROMA OF THE MEDIASTINUM REQUIRING SURGICAL INTERVENTION FOR RELIEF OF OBSTRUCTIVE SYMPTOMS. T. F. RIGGS and L. P. GOOD, Arch. Surg. **19**:309 (Aug.) 1929.

An unusual case of a ganglioneuroma, arising from the cervical sympathetic trunk, is reported by Riggs and Good. A boy, aged 4, with difficulty in breathing and fulness in the right anterior part of the neck, as well as a Horner's syndrome on that side, was admitted with a diagnosis of a large thymus. A roentgenogram showed displacement of the trachea and a mass in the upper part of the thorax. At operation, a mass attached to the thyroid and sympathetic trunk was removed; pathologic study proved this to be a mass of nerve fibers studded with ganglion cells. The patient died a year and a half after the operation. Mediastinal tumors are rare, and those arising from the sympathetic nervous system are the most rare.

DAVIDSON, Philadelphia.

URINARY CALCULI IN INFANCY AND CHILDHOOD. MEREDITH F. CAMPBELL, J. A. M. A. **94**:1753 (May 31) 1930.

Urinary calculi must be considered when chronic pyuria of childhood is present. This pyuria often leads to the diagnosis of chronic pyelitis and treatment by internal medication for months and years is unsuccessful. All children with persistent pyuria of more than four weeks after intensive medical therapy has been instituted should be subjected to a thorough urologic examination. In a certain number of these cases stone will be disclosed, and in nearly all some form of major disease of the urinary tract requiring special treatment will be found. The operative treatment for stone is as satisfactory in children as in adults and should be employed without hesitation when there is evidence of injury to the urinary tract or when further migration of stones with expulsion seems unlikely.

BONAR, Salt Lake City.

PAROXYSMAL TACHYCARDIA IN AN INFANT. MILDRED VAN CLEVE, J. A. M. A. **94**:1758 (May 31) 1930.

A case of paroxysmal tachycardia occurred in an apparently healthy infant, aged 7 months, with no other evidence of cardiac disturbance.

BONAR, Salt Lake City.

THE RELATION BETWEEN GROWTH AND SEASON IN CHILDREN. K. LANGE, Arch. f. Kinderh. **89**:259 (Feb.) 1930.

In 110 children in the second year of life the maximum growth was in the fall, the average in the spring and the minimum in the summer. The same was true of 54 children from 3 to 6 years of age.

SANFORD, Chicago.

A CASE OF INTRAPLEURAL CYST IN AN INFANT. HANS BISCHOFF, Ztschr. f. Kinderh. **48**:447, 1929.

A girl, aged 6 months, had had coughing spells for one week, becoming blue and unable to breathe; between the spells she showed retraction of the ribs. There was no vomiting. On admission to the hospital she was thin, flabby and slightly cyanotic, and showed some retraction. Percussion was dull at the base of the right lung posteriorly and râles were audible. The tuberculin test was negative.

The day after admission the dulness was greater, but feeble breath sounds could be heard. Roentgenograms showed an intense, homogeneous shadow on the right side, with the heart pushed to the left, and the right side of the diaphragm not moving. Puncture yielded 250 cc. of a light yellow, creamy exudate with a specific gravity of 1.008 and containing more leukocytes than lymphocytes. For a few days the patient's condition improved; then she became restless and short of breath. A second puncture yielded 200 cc., and a third puncture, nine days later, 125 cc. At autopsy extensive bronchopneumonia with fibrinous pleuritis was found on both sides; in the right pleural cavity there was a large paravertebral cyst, the wall of which showed the structure of the wall of the stomach; it must have been an embryologic outpocketing of the digestive tube.

EMERSON, Boston.

THE INHERITANCE OF ACQUIRED CHARACTERS. G. SACHAROFF, Med.-Biol. J. (Moscow) **5**:5, 1929.

In mice of from 5 to 6 weeks of age the spleen was removed and after this careful whole and differential blood counts were made from time to time. In the splenectomized animals a leukocytosis develops which persists for from ten to twelve months. When the splenectomized animals were interbred, the F_1 generation also showed a leukocytosis, but less marked than in the parental generation. F_2, F_3 and F_4, on the other hand, showed a leukopenia. When the spleen was removed from both animals in the F_1 generation, the F_2 generation showed a tremendous variation in the number and type of cells. When animals were crossed in the F_2 generation, the F_3 generation showed a very marked leukopenia and the animals died within a very short time.

The author interprets this result as follows: The leukocytosis in the splenectomized animals is due to the overcompensation by the hematopoietic system. The persistence of the leukocytosis in the F_1 generation is due to the transmission of the tendency to overcompensation. However, the fundamental reaction after the splenectomy is leukopenia; and the F_2 generation gives the normal biologic reaction. Both the tendency to leukopenia and the tendency to overcompensation are transmitted in the germ plasm with the result that the extreme reaction to overcompensation spends itself very soon and the fundamental biologic reaction comes to the surface. The fact that, when the mice of the F_1 generation were splenectomized and interbred, the F_2 generation showed a much greater leukopenia, is a proof of the author's contention, as shown by the formula that crossing DR with DR, one gets mostly DRs. It is significant that transmission of the acquired characters takes place through the mother.

KASANIN, Boston.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

JOSEPH BRENNEMANN, M.D., *Presiding*

Forty-Second Annual Meeting, June 17-19, 1930

(*Concluded from page 695*)

Fourth Session

Morning, June 18

COMPOSITION OF BONE: X. MECHANISM OF HEALING IN EXPERIMENTAL RICKETS. DR. BENJAMIN KRAMER, M. J. SHEAR and JAC SIEGEL.

In active, uncomplicated rickets a diminution in inorganic serum phosphorus is generally noted; the amount of serum calcium is usually normal. When no decrease in the inorganic phosphorus is observed in active rickets, the calcium concentration is usually below normal. These generalizations were expressed in a roughly quantitative form by the empirical Ca × P product of Howland and Kramer (*Tr. Am. Pediat. Soc.* **34**:204, 1922; *Monatschr. f. Kinderh.* **25**:279, 1923).

When healing of rickets occurs, resumption of calcification is usually accompanied by an increase in this empiric product. The present experiments were designed to determine whether the resumption of calcification precedes or follows the rise in the Ca × P product in the healing of experimental low-phosphorus rickets in rats.

Rickets was produced by means of three diets which had Ca : P ratios of 4.3 : 1, 6.1 : 1 and 17.5 : 1, respectively. In all cases the rickets was accompanied by a Ca × P product of 30 or less. Biologically assayed cod liver oil was added to the ration after rickets developed, and autopsy was performed on groups of rats at frequent intervals subsequently until calcification appeared in the provisional zone.

The diagnoses of active rickets and of fresh calcification were made on the basis of immediate histologic examination of the tibia after staining with silver nitrate. The blood of each rat was collected separately. The serums were pooled after histologic examination had been made; only the serums of rats showing similar histologic changes were combined. The rats were killed without anesthesia. Precautions to avoid hemolysis were almost invariably successful; the few hemolyzed specimens were not used for phosphorus analysis.

Definite correlation was obtained between the Ca × P product and the resumption of calcification. Rickets was invariably accompanied by a product of 30 or less. Whenever new calcification appeared, the product was 40 or higher; new calcification was never obtained with a low product. Furthermore, the product rose before the resumption of calcification; it rose from the low, rachitic level to values as high as 51 before new calcification appeared.

Similar experiments with phosphate gave analogous results. Addition of phosphate to the ration produced a rise in the product during the first twelve hours; new calcification also appeared within twelve hours. In this instance, too, the rise in the product preceded the appearance of new calcification.

Analogous results were also obtained with viosterol. The addition of viosterol in an amount equivalent to the vitamin D added in the form of cod liver oil in the preceding experiments, produced a rise in the Ca × P product from the

rachitic level of 21 to a value of 34 before healing occurred. By the time healing occurred, the product had risen to 49.

In this study, in which more than 350 rachitic rats were examined, the following points stand out: 1. In low-phosphorus rickets of rats, the Ca × P product was always 30 or less. 2. The healing of the rickets never preceded the rise in the Ca × P product. 3. The product rose before new calcification appeared. When the product was raised above 40, calcification followed rapidly.

The theoretical implications of this empiric product have been discussed in previous communications (Kramer, B., and Shear, M. J.: J. Biol. Chem. **79**:125 and 147, 1928; **86**:677, 1930).

THE RELATION OF TETANY TO HEALING RICKETS. DR. BENGT HAMILTON.

Rabbits were made rachitic with the McCollum diet 3143. A sample of blood was taken and the amounts of phosphorus and calcium in the serum were determined. Treatment with cod liver oil (1 cc. daily), viosterol (1 cc. daily) or ultraviolet rays (three treatments of five minutes at 20 inches [50.8 cm.]) was then instituted. After a few days a second sample of blood was taken and the amounts of calcium and phosphorus in the serum were determined.

The experiments show that as an initial effect of treatment a more or less marked decrease of the serum calcium often occurs. The blood picture in several cases was similar to that in infants with severe tetany, although no clinical signs of tetany were observed.

A similar blood picture (with low serum calcium) was occasionally found in rachitic rabbits showing roentgen evidence of spontaneous healing.

THE UTILIZATION OF INGESTED CALCIUM SALTS. DR. P. C. JEANS

It has been shown definitely that dental caries can be arrested or prevented merely by the ingestion of a general diet complete in all known essentials. American diets, especially those containing only small amounts of milk, are likely to contain less than the minimal requirements of calcium. This deficiency affects the child more than the adult, not only because the child requires from two to three times as much calcium as does the adult, but also because the calcium of certain foods, particularly vegetables, is less readily utilized by the child. Without doubt, this widespread use of diets deficient in calcium is one of the factors contributing to the prevalence of dental caries in this country. To remedy this defect, several preparations, mixtures of salts of calcium and phosphorus, have been recommended as of value in supplementing the mineral intake. The use of certain of these preparations has been advanced by fairly extensive propaganda, especially among dentists.

Little information could be obtained from the literature regarding the effect of the ingestion of various salts of calcium and phosphorus on the retention of these elements by children. Metabolic experiments were therefore undertaken in order to determine, if possible, the value of such mineral supplements in increasing the calcium and phosphorus retentions of normal children. For this purpose, two proprietary preparations were chosen. One of these is sponsored by Dr. Sherman Davis, under the trade name of Vicaperol. Each capsule contains, in addition to a small amount of cod liver oil and dried parathyroid, 43 mg. of calcium and approximately half as much phosphorus, both of which are purported to be in organic form, and therefore readily absorbable. The other preparation is sponsored by Dr. T. B. Wagner and contains calcium and phosphorus in the proportion of 4:3, approximately that of milk. The phosphorus is in the form of an organic phosphate and is obtained from corn products. Twenty-three of these tablets are equivalent in calcium and phosphorus content to a quart of milk.

The Davis capsules, in quantities equivalent to the calcium in 1 pint (5.5 liters) of milk, (fifteen capsules, or from three to five times the recommended dose), added to a diet containing only sufficient calcium to prevent loss increased the

retention of both calcium and phosphorus, but the retentions, despite the large intake, were far below the average retentions of these same children on the regular hospital diet containing 1 quart of milk (1.1 liters). Enough capsules could not be given to be equivalent to the calcium content of a quart of milk.

The experiments with the Wagner tablets were divided into three parts: (1) a basal diet plus a quart of milk, (2) a basal diet without milk but containing the protein equivalent of the diet given in period 1 and (3) the diet given in period 2, plus tablets equivalent in calcium and phosphorus to a quart of milk. Period 1 showed retentions of calcium of from 0.3 to 0.4 Gm. Period 2 showed a loss of from 0.4 to 0.5 Gm. In period 3 the output equalled the intake. Although the intake was quantitatively identical in periods 1 and 3, a sufficient retention of calcium and phosphorus for growth occurred only in period 1.

Though the children studied showed some utilization of calcium and phosphorus when administered in the form of mineral salts and in massive dose, this does not appear to be a practical method of supplying the calcium and phosphorus deficiencies of a poor diet. The ingestion of a quart of milk a day still remains the best method of insuring an intake of these elements that will favor adequate retention.

DISCUSSION

Dr. Edwin T. Wyman: While all patients with tetany have more or less severe rickets and, as Dr. Hamilton has shown, while tetany may develop in many cases of healing rickets, it seems to me that all patients with tetany do not have healing rickets. Other factors may cause tetany, principally, I think, infection.

If an infant with severe rickets acquires an infection, the calcium content may be so lowered as to precipitate tetany.

When this study was begun, we had difficulty in finding cases of rickets in the hospital owing to the infrequency of the disease in the early winter; it was therefore necessary to include infants with both rickets and tetany. Many of these patients are brought to the hospital because of convulsions. On examination, the infant will show perhaps an infection of the upper respiratory tract, tetany and rickets. During the period of observation in this series, without antirachitic treatment, subsequent blood determination and roentgenograms did not show healing of the rickets. In fact, in many cases the rachitic process was stationary or was becoming progressively worse.

Dr. L. R. DeReus: I should like to ask Dr. Hamilton (1) how the span of life in the rabbit compares with that in the rat and (2) with what promptness rachitic changes are produced in the rabbit as compared with the rat.

Dr. B. Raymond Hoobler: I should like to ask Dr. Jeans if the amount of calcium that the children retained was not far above the optimal amount that he suggested a child needed, about 1.5 Gm. daily. I think that the charts showed twice or three times that amount. Is it well, therefore, to attempt to administer that much calcium, even though it is retained well on a milk diet?

Does he think that in addition to a regular diet a child should be given 1 quart of milk a day even though this increases the calcium? Are there not other factors connected with the feeding of a full quart of milk plus the fat and some of the other constituents that might operate against the value of the total amount of calcium retained?

In other words, I do not think that a child should be given a full quart of milk a day plus the average food. In my experience with nutritional conditions in children, a pint of milk a day is much better than a quart.

Dr. Hamilton: I should like to ask Dr. Jeans what it is in the milk that makes it a suitable medium for the absorption of calcium. Is it the buffer of milk, or the protein that stimulates the secretion of acid in the stomach?

Dr. Lynne A. Hoag: I was interested in Dr. Hamilton's point concerning the increase in phosphorus content during the treatment of rabbits for rickets, because this corresponds with observations on tetany in infants. As was pointed out in Dr. Schloss' clinic, of the last eighty cases of tetany showed phosphorus

levels above 7 mg.; this would seem to fit in well with the observations that Dr. Hamilton made on healing rickets in rabbits.

Dr. Hamilton: I agree heartily with Dr. Wyman's statement. I am sure that infection is an important factor in causing tetany and I have been wondering whether the mechanism may not be the same as that in the tetany produced in rachitic rats by starvation; in the latter instance the rats live on their own body tissues and thus secure a large supply of phosphorus from their own muscles. I wonder if increased combustion of body tissues in infection might have the same effect. That is a theory, but I am sure that Dr. Wyman is correct in saying infection may cause tetany.

We produced rickets in 100 per cent of the rabbits that we put on the diet, but the response varied. As to the span of life, I have no comparative data.

Dr. Hoag referred to the increase of phosphorus in rats. I am sure that this has also been observed. It is, I think, connected in some way with the fact that by giving phosphorus, one can produce severe tetany in experimental animals.

Dr. Jeans: I did not wish to enter into a discussion concerning the quantity of milk desirable in a child's diet. I do not believe that there is any sanctity in the amount, whether a pint or a quart. I do not believe that the optimal calcium retention intake is known.

I think that it has been shown fairly well that calcium retention is increased in children with the increase of ingestion until approximately 1.5 Gm. of calcium has been taken. Whether this is an optimum or merely a maximum has never been determined.

The diets that we customarily give these children contain, exclusive of milk, between 0.2 and 0.4 Gm. of calcium. A quart of milk adds 1.2 Gm. This brings the total to approximately 1.5 Gm. of calcium as the daily intake. This same diet, including only a pint of milk, contains approximately 0.9 Gm. of calcium. I question whether the latter amount is sufficient to permit an optimal retention of calcium.

A number of factors enter into the determination of a sufficient intake of milk, factors that represent entirely different points of view. The effect of the ingestion of milk on appetite has been discussed extensively, but the daily calcium intake receives entirely insufficient consideration.

I wish that I could answer Dr. Hamilton's question as to what it is in milk that causes the calcium to be better utilized than it is from certain other sources. It is well to realize that milk is the only food that has a high calcium content. It is chiefly for this reason that calcium retentions are better when milk is included in the diet than when it is not.

Sugar and Phosphorus Relations in Blood Glycolysis. Dr. George M. Guest.

There is a considerable amount of evidence that phosphorus plays an important rôle in the metabolism of carbohydrate in the animal body. This is traced principally in the fluctuations of the inorganic phosphorus of the blood during tests of dextrose tolerance, and in the studies of the hexose-phosphoric acid compound, lactacidogen, in the muscle identified by Embden as active in the chemical mechanism of muscle contraction. Harden demonstrated that the presence of phosphates is absolutely essential for the alcoholic fermentation of sugar by yeast, and that the conversion of sugar to alcohol, carbon dioxide and water is brought about by the intermediate formation of hexose-phosphoric acid esters. The present experiments were conducted to trace relative changes in the phosphorus and sugar of the blood in glycolysis that might indicate the occurrence of chemical reactions comparable to those outlined by Harden as characteristic of alcoholic fermentation.

Samples of the blood were defibrinated and incubated at 37° C. Measurements of the sugar and inorganic phosphorus content (in some experiments, the other phosphorus fractions: total, total acid-soluble, lipin) were made at hourly or two-hourly intervals over periods of from six to twenty-four hours.

Glycolysis occurs in normal blood at a regular rate, equivalent to a loss of about 15 mg. per hundred cubic centimeters per hour until there remains a residual reducing substance of about 20 mg. per hundred cubic centimeters. During this period the inorganic phosphorus remains at a constant level or it may diminish slightly. At the time the free sugar is exhausted (in from six to eight hours) the inorganic phosphorus rises sharply and progressively to reach a concentration of about 20 to 25 mg. per hundred cubic centimeters at about the fifteenth hour. This rise in inorganic phosphorus is at the expense of the organic acid-soluble phosphorus fraction, identified by others as hexose-phosphoric and glycerophosphoric acid esters contained within the cells. The rise occurs very quickly in the hypoglycemic blood of insulinized animals, and it is delayed for several hours by the addition of an excess of dextrose or levulose to either normal or hypoglycemic blood. The process thus visualized is probably as follows: Free sugar combines with free inorganic phosphorus to form hexose-phosphoric acid esters in the cells. As the glycolytic enzyme splits the sugar molecule (first to two molecules of lactic acid), the phosphorus is liberated in free form to combine again with free sugar. When, however, the sugar is exhausted, the inorganic phosphorus is seen to increase in concentration since there is continuous hydrolysis of the esters and no free sugar is available for their resynthesis.

The curves plotted to represent the glycolysis and phosphorus-hydrolysis are characteristic and fairly constant for samples of normal blood, but this cycle of changes observed in normal blood is markedly disturbed in certain pathologic conditions, as in the gastro-intestinal intoxication of infants and in nephritis with severe acidosis. In these states there is a rapid rise of the inorganic phosphorus (that is, hydrolysis of the organic acid-soluble phosphorus compounds) observable from the time the blood is withdrawn from the body and independent of the glycolysis. The reaction of the blood plays an important part in governing these changes.

DISCUSSION

DR. SAMUEL AMBERG: In one case the reaction seems to be the rapid rise in phosphorus content; in the other instance, the increase takes several hours. Might not the second case, in which there is a latent period, be an autolytic process? The glycolytic reaction seems to proceed without a latent period, while the one liberating the phosphorus may have a latent period. These conditions suggest the possibility of reactions of a different order and therefore a lack of correlation, at least under certain conditions.

DR. ALEXIS F. HARTMANN: Did Dr. Guest try to reverse his study, particularly with the idea of determining whether inorganic phosphate always diminishes following the administration of dextrose? I ask that because I have been interested in a similar problem.

When lactic acid or sodium lactate is given to human beings or animals, a remarkable drop in inorganic phosphate is sometimes seen, but this is by no means constant. Apparently in infants and in animals that are starving and lack a glycogen reserve, there occurs a rapid combination of lactic acid with inorganic phosphate, whereas in children or animals that still have a good glycogen reserve, no such change takes place, the lactic acid being oxidized and not converted into glycogen.

DR. BENJAMIN KRAMER: I should like to ask Dr. Guest what happens to serum separated from the corpuscles. Serum contains plenty of sugar, but very little, if any, so-called acid-soluble phosphorus in excess over inorganic phosphorus.

DR. GUEST: The factors that control these reactions are by no means understood. Synthesis and hydrolysis of the organic acid-soluble phosphorus substances proceed simultaneously, and shifts of reaction toward acidity apparently inhibit synthesis, leaving the hydrolysis most in evidence. The shift of reaction is, however, probably only one of several factors affecting this cycle of changes.

Dextrose administered to a normal person, either by mouth or intravenously, causes a slight depression of the inorganic phosphorus of the blood. Insulin

causes the same change. This depression is, however, not observed in states of severe acidosis or in nephritis, in which high values of inorganic phosphorus are found in the blood. Likewise in these conditions the addition of sugar in vitro to samples of blood did not cause a diminution of the inorganic phosphorus or slow the rate of its hydrolysis.

Glycolysis does not occur in serum that is obtained with precautions to prevent the admixture of cell substances. Such serum contains only from 0.2 to 0.5 mg. per hundred cubic centimeters of acid-soluble phosphorus; on standing, the maximum rise in inorganic phosphorus will be no more than this amount. In serum standing in contact with cells the inorganic phosphorus will be found to increase rapidly. Likewise, if blood is treated in such a fashion that the organic acid-soluble phosphorus escapes from the cells, a considerable increase in inorganic phosphorus will be observed as the serum stands.

A Study of the Water and Mineral Metabolism of Epileptic Children on Diets High in Carbohydrates, Proteins or Fats. Dr. Frederic H. Bartlett, Dr. Kenneth M. Metcalf and Dr. Ruth Fox.

This paper covers a study of the effect of various diets on water and mineral metabolism. A high carbohydrate diet favors a retention of water in the body with a gain in weight while a high protein or a high fat acid ash diet favors the elimination of fluid with a loss of weight. A high dextrose diet also favors the elimination of fluids.

An analysis of these diets shows that the high protein and the high carbohydrate diets are high in minerals and water, while the high fat acid ash and dextrose diets are low in minerals and water.

A study was made of the mineral balance of children with epilepsy on various diets. The high protein diet causes a marked retention of all minerals, but especially of potassium and sodium. The high fat acid ash diet, however, shows a negative balance in calciums, sodiums and chlorine. The dextrose diet shows a negative balance in calcium and a slight positive balance in sodium and chlorine.

The minerals in the blood show similarly a drop in calcium, sodium and chlorides on the high fat acid ash and dextrose diets, this being especially marked in the dextrose diet in which there is a drop of almost 25 per cent in chlorides. On high carbohydrate and high protein diets the blood minerals show no drop.

From a clinical point of view the high fat acid ash diet and the high dextrose diet are the most effective in the control of convulsions, while the high protein and high carbohydrate diets are the least effective. It is significant that the diets that lessen the frequency of attacks are the diets that contain the least minerals and, of course, the least water.

If the elimination of fluids was the only factor in the control of attacks the high protein diet should have the best effects because it causes the most marked excretion of fluid. Its ineffectiveness may be due to its high mineral content.

In epilepsy, the good effects of the high fat acid ash diet have been demonstrated; on the other hand, the good effects of a high dextrose diet have yet to be substantiated. Our studies to date lead us to believe that the high dextrose diet is equally effective in the control of convulsions.

DISCUSSION

Dr. Bengt K. Hamilton: Through the work of Dr. McQuarrie, it is becoming increasingly clear that the amount of body fluid is in some way connected with seizures in epilepsy, and that there are, fortunately, many ways in which the body can be deprived of superfluous fluid. If one of those methods does not work, one can use another.

The work done by Dr. Bridge of Johns Hopkins Hospital practically illustrates this point. Two patients with petit mal had been on the ketogenic diet for a long period. In one case the attack completely disappeared; in the other the diet was ineffective. Both patients were given a starvation diet. Gamble and Ross have shown that this is one way in which the body can be deprived of fluid. In the case in which the diet was effective, there was no loss in body fluid as measured

by the weight or sodium output, which is also an indication of loss of body fluid. The curve for weight and for sodium output was almost horizontal. The case in which the diet had not been effective showed a marked loss of body fluid, and coincident with that loss the attacks disappeared. When the starvation diet was stopped, the patient was placed again on the ketogenic diet; the attacks did not come back. Obviously, in that case, the ketogenic diet had been ineffective in dehydrating the body and, consequently, ineffective in preventing attacks. The ketogenic diet alone had not dehydrated the body, but when starvation was imposed, the body lost its fluid and remained dehydrated, and the patient remained free from attacks.

I think that Dr. McQuarrie deserves great credit for pointing out the intimate connection between body fluid and attacks in epilepsy.

Dr. Henry F. Helmholz: I have been much interested in both of the papers mentioned, in so far as they give a clue to the possible factors that control convulsions.

I have observed several patients who have been dehydrated to the point where the mouth was dry and there was an elevation of temperature, without any control of the convulsions. One of those patients was later put on the ketogenic diet with complete control of the convulsions, which has continued for a period of four months. I have also been making some experiments in acute dehydration with sucrose solutions. The work that Dr. Keith has been doing shows definitely that convulsions can be prevented on a standard dose, and that from two to three times the usual dose will be tolerated after dehydration; also that certain ketone bodies, such as acetol, ethyl aceto-acetate diacetone alcohol have a definite effect in controlling convulsions.

I have observed several patients with epilepsy, especially petit mal on a controlled ketogenic diet, who apparently can take an almost unlimited amount of water and still remain free from convulsions.

It has therefore seemed to me that although the water factor was important, it was not necessarily the only active factor in the control of convulsions.

Further Studies on the Water Exchange in Epileptic Children. Dr. Irvine McQuarrie.

Simultaneous measurements of the water and mineral balances of the body have been made in a series of children with epilepsy under a variety of carefully controlled conditions. Isocaloric, high fat, high protein, high carbohydrate and borderline diets have been tested in succession on the same patient in regard to their specific effects on the water and mineral exchanges and on the occurrence of convulsive seizures. The effects of varying the state of hydration of the body in patients on constant diets and comparatively high water intake by the administration of diuretics, cathartics, an antidiuretic (pituglan) or extra water have also been determined.

A negative water balance, no matter how produced, was usually accompanied by a negative sodium and chlorine balance and by the cessation of seizures in subjects with severe attacks of epilepsy. The effects on magnesium, calcium, phosphorus, sulphur, and nitrogen were variable. With the reestablishment of a positive water balance, sodium and chlorine were stored and seizures tended to recur. On a diet comparatively low in sodium chlorides, prolonged pituitary antidiuresis resulted in a proportionately greater retention of water than of sodium, potassium and chlorine. Seizures recurred regularly under these conditions.

One patient who responded satisfactorily to a ketogenic dietary regimen without water restriction, showed strikingly negative water and chloride balances; whereas, another whose seizures were not entirely prevented by a regimen practically identical with this showed an almost even balance between intake and output of water and chlorine and stored sodium. The total excretion of acetone

bodies was approximately twice as great in the former case as in the latter. One patient was observed in whom convulsive seizures, occurring in series at weekly intervals, could not be prevented by the administration of phenobarbital alone, by a ketogenic diet or by restriction of the water intake. Sodium bromide in large doses prevented seizures entirely. Mineral analyses on the excreta from this patient have not been completed as yet, but yield sufficient information to explain her anomalous response.

In comparing the reaction of nine children with mild epilepsy and equal number of children without epilepsy to frequent administrations of water and ampules of pitressin, it was found that all but one of the former had convulsions within from fifteen to thirty-six hours, whereas none of the latter had seizures, although their increase in weight owing to water retention, was as great or greater than that of the children with epilepsy. This procedure is therefore tentatively proposed as a diagnostic test for epilepsy in questionable cases.

Discussion

Dr. McQuarrie: I agree with Dr. Helmholz that dehydration is not the only factor in the control of seizures by regimen.

As I have just shown, two patients were in the metabolism ward at the same time on the same regimen. One responded well to the ketogenic diet and the other rather poorly. They were given practically as much water as they wished. The one who responded satisfactorily was dehydrated; the other was not, although the water intake was the same. There were other differences also, particularly in the method of handling the minerals. The child who showed the negative water balance likewise showed a negative sodium and chlorine balance, whereas the other did not.

We recently summed up the work of three years on the lipid changes of the blood plasma in epilepsy. While changes in lecithin and cholesterol separately do not always appear to be present, the ratio, cholesterol, apparently has an interesting relation to the occurrence and frequency of seizures. I think that this may be one of the factors, as it is thought to be related to permeability of cell membranes. The ratio tended to be highest when seizures were most frequent. I do not believe that one can as yet lay down any one principle for the treatment in all cases.

Fifth Session

Evening, June 18

A New Cereal Mixture Containing Vitamins and Mineral Elements. Dr. Frederick F. Tisdall, T. G. H. Drake (by invitation) and Mead Brown (by invitation).

This article appears in full in this issue, p. 791.

Discussion

Dr. Warren R. Sisson: I think that the paper that Dr. Tisdall has presented is one of considerable importance. I should like to ask him whether the germs of various grains differ very much in the content of iron and vitamins; in other words, is the content of the corn more valuable than the content of the germ of wheat?

The following case, which I think Dr. Van Ingen saw and which Dr. Clifford and I hope eventually to report, is mentioned merely to emphasize what I consider really important, the lack not only of vitamin D but of vitamin B.

A year before the present meeting, a child, aged 12, was receiving excellent care from physicians in New York; later he was at his parents' summer home. They were people who had every advantage, possibly too many advantages. Possibly three or four months before we saw the patient, a well defined case of what we propose to call pellagra beriberi had developed, of which she ultimately died.

There were definite cutaneous signs of beriberi, disturbance in gait and later virtual paralysis. The patient responded miraculously to large doses of brewers' yeast; after two weeks on a mixed diet with brewers' yeast her condition improved, but she died suddenly from an infection, a frequent occurrence in a deficiency disease.

DR. B. RAYMOND HOOBLER: Dr. Tisdall has worked out an interesting problem that we have all been anxious to see investigated.

There is hardly a day that the physician's mail does not include an advertisement of a cereal or sugar that contains or is supposed to contain a certain amount of these vitamins. Even in the chain stores now, there are packages of cereals marked with the vitamin B content, vitamin A content, etc. In fact, there are cereals called ABCD on the market, so that one can supposedly supply all the needs of the body. These products, however, are in the hands of the commercial manufacturers, and one should always be on one's guard against misrepresentation. On the other hand, the cereal described has been put together scientifically.

I should like to ask Dr. Tisdall a few questions about it: 1. With the quantity of wheat germ that it contains, will the cereal keep? One of the difficulties of putting wheat germ on the market at the present time is its inability to remain on the shelf for some time without the development of weevil or some form of rancidity. It is therefore extremely important to consider the keeping quality. *2.* What does it cost? Can it be put on the market at a reasonable price, so that physicians can recommend it to mothers generally as a cereal good for their children? Dr. Tisdall said that it had been used in the hospital for three months and that it had produced no bad results. I am sorry that he could not have said that it had been used for three months with certain good results. I hope that in another year he will at least give these good results. I think that there is too great a tendency to use animal experimentation and to attempt to transfer the procedure to children. I have no doubt but that Dr. Tisdall will show, before long, the positive benefits to be obtained from a cereal of this kind.

I think that vitamin D should never be used to replace cod liver oil or viosterol.

I thank Dr. Tisdall for the splendid work that he has done on a much needed project for children.

DR. BENJAMIN KRAMER: The striking difference between the degree of antirachitic potency of brewers' yeast subjected to solar irradiation and that exposed to irradiation with the mercury vapor lamp is interesting. If my memory serves me correctly, others have had quite different results, and I wonder what evidence there was that the lamp used in irradiating this material was potent.

DR. JULIUS H. HESS: I am going to ask a question of all the members present, which Dr. Tisdall is anxious to have answered. He stated that in the part of Canada in which he resides there is a decided deficiency of sunlight during nine months of the year. He stated to me that he is uncertain as to whether he is justified in irradiating either the wheat germ or the yeast employed in his cereal mixture, thereby adding another food product high in vitamin D to the diet of the infant and child. Dr. Tisdall will welcome suggestions from the members.

DR. TISDALL: Dr. Sisson asked: Does the germ in the various grains differ in iron and vitamin content? Unfortunately I cannot answer that. I understand that wheat germ is the only germ that contains vitamin E in an appreciable amount. From the practical standpoint, wheat germ is the only germ that is available in large quantities. As I have said, it is owing to a desire for the finely milled product that the wheat germ is carefully separated as being unsuitable for human consumption and is fed to chickens and hogs.

With regard to Dr. Hoobler's question about the keeping quality of the wheat germ, the cereal mixture that we have used is dried at a temperature of 70° C.

which takes out a great deal of moisture and kills any of the eggs of the weevil, etc., which are present in all whole grain products. The cereal has been in large barrels in the basement or in the store rooms of the Hospital for Sick Children for about three months and is fresh and sweet at the present time. We feel that it will keep indefinitely if it is dried and partially sterilized, as one might say, to kill the eggs of weevils.

The cost of this product should not be great. It should be possible to have it made commercially at a slightly greater cost than the cereal products made of white flour in granular form that are widely used for infants. There is nothing about it that should make the cost prohibitive.

Dr. Hoobler stated that we had inferred we had no bad results. I concluded my remarks by stating that we felt that this mixture should prove of definite value because it contained so many elements that are known to be necessary for normal nutrition. We have been so busy in the last six months, trying to get this mixture together and to carry out the animal experiments, that we were not able to make observations on human subjects other than to see that the infants would take the product and that it did not upset them in any way. We are making further observations on the effect of feeding this product to infants and children.

Dr. Kramer asked whether these lamps were potent. The lamp cost $600; it was the best Victor Lamp that we could buy and was quite new. Wheat germ has not the amount of viosterol that dry brewers' yeast has. I believe that if we put dry brewers' yeast under the lamp as we did wheat germ we would produce the same potency as by exposure to the sun. The surprising thing is the extremely high potency of vitamin D obtained by the irradiation of yeast with sunlight.

I am sorry that there are no more comments on the vitamin D content of the cereal mixture. Our own feeling is that this product should contain some vitamin D. No claim should be made that it prevents rickets; it would have a tendency to prevent rickets in cases in which an ordinary cereal has a tendency to produce rickets, and it would thus act as an aid to cod liver oil or viosterol.

THE SELF-SELECTION OF DIETS BY INFANTS. DR. CLARA M. DAVIS.

The experiment in self-selection of diets by infants has been carried on for four and a half years for the purpose of studying what and how much infants of weaning age would choose to eat and what would be the effect on them. A list of simple, unmixed foods, comprising meat products, sea fish, eggs, vegetables, cereals, fruits, sweet and fermented lactic milk and sea salt, has been prepared, of which from eight to eleven dishes are offered to the infants at each of three meals a day.

The infant chooses his own food from a tray set before him; emptied dishes are refilled so that he eats what and how much he chooses without interference. Records of the physical condition of the infants, as well as of the quantities and kinds of food eaten at each meal, have been kept. The infants eat their meals eagerly but without haste. Their tastes have varied widely in the group, and each infant has varied his choice of foods to a great extent, occasionally passing through "waves" of maximum consumption of a particular food. No attention is paid to table manners and each infant eats in any way that he can, the nurse assisting only the smallest infants who are not yet able to use their hands. These infants have eaten more than has usually been thought good for babies of their age. They have not standardized their choice of kind or quantity of food, and we are unable to predict what or how much an infant will eat at a meal. Considered over a given period, their diet in terms of protein, carbohydrate, fat, calories, acidity and alkalinity shows a reasonable picture, though not one that agrees perfectly with accepted ideas of what these should be. Two of the infants had rickets at the time of their admission to the hospital. Roentgenograms showed healed rickets in both before the end of six months. One took some cod liver oil and the other, none. Neither infant had sun baths or light treatments.

The questions why the infants have chosen what they have and why they have maintained health and growth at least equal to the highest standards are as yet unanswered. The experiment, which still remains an experiment, suggests, however, that the infant's likes and dislikes can be made a help instead of a hindrance in his feeding, and that it is a question whether or not it is sound practice to specify too rigidly regarding the quantity of food to be eaten and the manner of eating it or that interference and diversion need accompany each meal.

DISCUSSION

DR. HENRY DWIGHT CHAPIN: The study of nutrition in infancy has been one of the objects of the American Pediatric Society since its origin. I was one of the charter members of this society, so that I have followed all kinds of theories on food and digestion. I imagine that some of the fathers of pediatrics would have had an uncomfortable moment in seeing these pictures. One can learn from these experiments that the food likes of animals are important in nutrition.

Several years ago, before this society, I read a paper on the limits of chemistry in infant feeding. Later came the idea of calories, the limitation of calories affecting infancy. Students were figuring the calories and feeding the babies all sorts of things if the calories were right. One can use sawdust and water and have the calories satisfactory. That does not mean that the chemistry and calorie system are not of great value, but they were overstressed.

I studied the idea in animals. The agricultural experiment stations made a great many experiments in animal nutrition, much more careful than those made on human beings. They found that a consideration of the chemistry of food was not enough. The animals would not always take the rations, and the food likes of animals must always be followed. The real science, after all, is trial and error, and as success needs no apology, I can imagine that we must pass children. One can learn that the likes and dislikes of a person have a great value in nutrition. By changing the flavor of meat broth one can induce a child to take it when it would otherwise reject it.

Dr. Davis was working with a more robust group of infants than I have generally seen. I feel that if I had given a child ten eggs, I should have been tempted to give a laxative.

DR. BRONSON CROTHERS: I should like to know if one could arrange to show that film. One of the great points about the practice of pediatrics is to educate the mother. I believe that it would be important to show mothers what happens when a child has a free choice of food.

DR. HOWARD CHILDS CARPENTER: One is especially impressed with the behavior of these children. They seem entirely free from the conditioning influences of the modern American home. The self-selection of diet is a positive measure for the prevention of anorexia. Dr. Davis' experiment is a real contribution to pediatrics.

DR. FREDERIC W. SCHLUTZ: Did any of the children show a marked preference for milk in the selection of their foods, and did they frequently take milk to the exclusion of the more solid forms of the diet?

DR. ROWLAND G. FREEMAN: Was there any restriction in the amount of sugar presented?

DR. LOUIS C. SCHROEDER: Did any opportunity develop to study perverted appetites, for instance, in children who ate plaster or dirt, known as pica?

DR. JOSEPH BRENNEMANN: I have known of this work almost since Donald and Abraham were given their first meals. Having been an eyewitness, I should like to give my impression. It has been interesting to see the different reactions that people have had to this work. I have talked to a number of persons regarding this. One pediatrician said: "She put a lot of food in front of the child and got away with it." When Dr. Davis came to Chicago, I was interested in

having her continue her work at the Children's Hospital. The attitude of the superintendent was interesting. She was a Canadian and she said that what was needed in the United States was better table manners instead of worse! My own reaction to it is that it is one of the most fundamental and far-reaching pieces of work that has been done in my time. It is not only interesting; it is practically valuable. By this I do not mean that it is a method to be used for feeding children at the present time. I think that Dr. Davis would like to have me emphasize the fact that this is a scientific experiment, and not a method of feeding.

As a scientific experiment, its greatest practical value lies in its action as a stabilizer, or a sort of purgative, of many ideas with reference to the feeding of children. Children should have something to say for themselves.

I think that every one who has listened with as much patience as he has been able to command to the stereotyped story that over 50 per cent of the patients in private practice present, that their children do not eat for the reasons that I mentioned, can appreciate this work as a fundamental contribution of the first rank.

The pictures are interesting but do not convey by any means the impression obtained from actually seeing the work. I know of no thrill in medicine that surpasses the one I have when I see eight or ten of these children sit down in perfect silence and begin their meal with the biologic abandon that ought to characterize the meals of all young animals, and that does so except in the case of the human young under present conditions.

Dr. Davis: In regard to Dr. Chapin's remarks, I did not feel that these were particularly robust infants. All except four were underweight, and some of them showed anemia. I shall be glad to talk to Dr. Crothers about the films; there are no duplicates.

In regard to Dr. Schlutz' question about milk, one cannot state an average figure for these infants, perhaps because they vary so much from time to time and among one another. Some infants have taken as much as 50 per cent of the total food intake in the first six months as milk, and others have taken none.

In regard to Dr. Freeman's question about the ingestion of sugar, let me repeat that no sugar is served. This is merely for the purpose of keeping the experiment in its simplest terms, no derived food products being used. We have tried to keep the experiment the same throughout without introducing other factors and to keep the children as long as possible. I presume that Abraham and Donald are among the few young men in the world who at the age of 4 and 3½, respectively, have never tasted sugar or had an ice cream cone. With regard to their having access to the things that children with perverted appetites eat, such as dirt, etc., they have had only such opportunities as come to every child. Occasionally, they have put sand, bits of plaster that they have picked from the wall, wood and paper in their mouths and, as most babies do, they have experimented with putting their toes into their mouths. We have not put dirt or other such materials on their trays, however, as in order to obtain definite ideas about the choices of the different infants we have kept the list of things the same throughout the experiment and have not tried mixed dishes, sugar and materials not commonly used as food, enticing as many of these things may be.

A Clinical and Experimental Investigation Concerning the Effect on Life and Growth of Complete Stricture of the Esophagus with Loss of Saliva. Dr. Joseph Stokes, Jr., and Dr. Theodore S. Wilder.

The effect of complete stricture of the esophagus on life and nutrition has been the subject of few investigations. Apparently few of the earlier clinicians or physiologists believed that closure of the esophagus had any serious effect on health. This belief was not the result of experimental investigation or of clinical experience, except in a few instances, since continued life after complete closure of the esophagus has been a rare occurrence.

Recently a number of investigators have studied this problem both clinically and experimentally, with contradictory results as to the effect of complete closure on life and general nutrition. To our knowledge, no investigation has been made concerning the effect of such closure on growth.

The subject of our clinical investigation was a girl, aged 10 years, with a complete stricture of the esophagus. On admission to the hospital, her weight was 41 pounds (18.6 Kg.) and she was extremely malnourished. This study was started forty-eight days after admission when she had lost 4 pounds (1.8 Kg.) despite various attempts at improving her condition. On account of her malnutrition those in charge felt that it was unwise to omit saliva from her food, so that no comparison of mineral and nitrogen balance could be made before and after saliva had been added. Her diet was increased and made more fluid; also her loss of saliva by expectoration between meals was gradually stopped. Her gain in weight was extremely rapid and the diet was increased according to this gain, which continued with the same rapidity despite the later removal of saliva from her food. Within eight months the gain of weight was 30 pounds (13.6 Kg.). We consider this as strong evidence against the hypothesis that complete lack of saliva in the stomach markedly impedes growth.

The experimental investigation of this hypothesis was carried out on nine young pigs, eight of which were of the same litter. The esophagus was brought out externally, and divided; the upper end was tied off or allowed to drain externally and the animals were fed regularly through the lower end. Despite several deaths among both the animals operated on and the controls, satisfactory gains in weight were obtained in the three animals surviving the operation, comparing favorably with one healthy control animal. All had the same caloric intake and equal quantities of water. We consider this also as evidence against the hypothesis that saliva is necessary for growth, and as evidence that acute experimental closure of the esophagus is frequently nonfatal.

THE INFLUENCE OF EXCESSIVE MILK FEEDING ON GASTRIC MOTILITY AND ITS RELATION TO CHRONIC ANOREXIA. DR. FREDERIC W. SCHLUTZ and DR. WALTER J. SIEMSEN.

There has been widespread propaganda for the extensive use of milk in the child's dietary. Its availability, simplicity of use, acceptability to the child and conceded excellence as a nutritive substance have all contributed to further this propaganda.

Contrary to the opinion and dictum of nutrition workers who base their conclusions largely on laboratory and animal experimentation, many pediatricians of large clinical experience are doubtful of the value of a considerable amount of cow's milk in the child's dietary. They feel that it is an important contributory factor in the causation or development of chronic anorexia in children beyond the age of infancy.

Czerny spoke of Milchnährschaden over twenty years before the present meeting. Nutrition experts are ardent advocates of liberal amounts of milk in the diet, especially for the growing child. Milk meets most of the requirements of a balanced diet. Numerous investigations with school children seem to point conclusively to the nutritional value of milk.

Definite ill effects from excess milk feeding have been described. It is a common clinical experience that children who take large amounts of milk in the diet to the exclusion of other foods sooner or later develop chronic anorexia. It is not clear whether the development of this phenomenon is due to deficiency in vitamin or mineral content of this food or whether it is due to the direct effect of the food itself on account of some peculiarity of composition or individual component.

A series of studies is under way to clear up these points. This particular study deals with the physiologic effect of prolonged excessive milk feeding on gastric motility.

Gastric motility studies and gastric analyses together with clinical observations were made before and after a milk diet. Gastric motility studies were also made after the ingestion of milk and compared with those in which no milk was ingested. The graphic balloon method of Carlson was used. The intensity of the child's gastric motor activity is intermediate between that of the infant and that of the adult. The children observed were older than 9 years and free from disease. They usually objected very little to taking the balloon and tube. Several tracings were usually necessary to gain a fair knowledge of gastric motility. The tracings were continued for about one and one-half to two hours at a time. The milk diet was continued for from ten days to two weeks. Milk was given ad libitum. In a few instances the emptying time of the stomach before and after a milk diet was studied. Records of gastric motility show great variability in different children. As a rule the asthenic child has less motor activity than the normal child. In general, it seems that the gastric motor activity was of about the same magnitude after the milk diet as before it. Decreased motility was observed more frequently after the milk diet than was augmented motility. Tracings taken after the ingestion of milk showed practically as great gastric activity as did those taken without the ingestion of milk. The average daily intake of milk was from 2 to 3 quarts (2.2 to 3.4 liters). The weight remained practically stationary. A definite decrease in appetite following the milk diet was not observed. In a few cases the appetite seemed greater than before the milk diet. The well-being of the children seemed unimpaired.

The study shows that excess milk feeding over a short period of time has little or no influence on gastric motility and that it seems to have no unfavorable influence on appetite.

DISCUSSION

Dr. B. Raymond Hoobler: Ten years ago, I read a paper before the Society on the misuse of milk. I attempted to show the wrongly balanced ration when a child was offered the average amount of food plus a pint of milk and plus a quart of milk. The charts presented at that time showed that with the average pint of milk the diet contained about 35 per cent fat, and with a quart of milk over 50 per cent fat.

The children whom Dr. Schlutz studied were given full milk diets, which would mean that they were obtaining from 50 to 52 per cent of the calories in the form of fat. It has been my experience that when that quantity of fat is fed to either a child or an adult, anorexia develops sooner or later. Whoever has had the experience of drinking a quart of milk a day remembers that it was not long before the edge of his appetite was worn off. The milk became distasteful and the entire diet nauseating. It has been my experience that either latent or open acidosis develops. Most of these children will show a low amount of acetone in the urine. It therefore seems to me that the greatest difficulty in feeding a large quantity of milk is in producing a state of latent acidosis or a condition that destroys the appetite.

Dr. Schlutz has taken up the problem in a different way. I am glad that it is being taken up. I think that such a common article of food as milk should have been studied more generally.

Dr. Franklin Paul Gengenbach: It has always seemed to me a mistake to allow the milk to be on the table at the time the child has its meal. For a great many years, I have asked the mothers to omit the milk at the time of the meal, starting in early infancy, and especially when the children are being taught to take other food. One reason why I adopted this method was that so many children drink the milk in order to gulp down the solid food.

It has also been my observation, as it must have been with most pediatricians, that in malnutrition it is usually a mistake to try to force the child to drink milk between meals. If anything has to be given, I give orange juice. It seems to me that the practical application of this observation is that the food must be taken as

dry as possible, and that the milk should be given only in the quantity in which the child desires to take it at the end of the meal.

Dr. Schlutz: In the cases studied it was of interest to note that, with one exception, none of the children who received large amounts of milk showed acetone in the urine. The average dairy milk of Minneapolis contains from 3.2 to 3.4 per cent fat. Milk with this fat content given to children over a long period does not cause marked retardation of motility.

As to the remarks of Dr. Gengenbach, I have had the same experience when the child is allowed to select its own food. It will almost invariably take milk in preference to solid food. I have found it advantageous always to keep the milk from children until they have taken all the other foods.

The Clothing of Infants. Dr. Charles Hendee Smith.

Proper clothing for infants should provide even warmth without overheating, ease of dressing and undressing, certainty of covering, freedom for exercise and adequate diaper care. The infant spends most of the time in bed; hence the manner of making the bed must enter a consideration of his clothing.

The usual shirt, band and petticoat of wool are often too warm; with the addition of slips, dresses, sacques or sweaters, the number of sleeves to be pulled on is often trying to both nurse and baby. A single layer of wool is enough except in cold weather.

A bed made up like that of an adult does not keep the infant properly warm because the bedding rarely covers the arms and shoulders and is easily kicked off. A visit to almost any hospital ward will show several babies uncovered and chilled. The addition of more sweaters and coats does not compensate for the failure to keep the shoulders covered. The experience of mankind has led to an almost universal practice in the matter of beds. Adults take off all their clothes, put on a single layer of thin cloth and get into an air chamber made by sheets and blankets. If this were not the best way to keep warm it would not be a general custom. Adults do not put on many layers of clothing and leave the arms and shoulders out. Why should the infant be dressed in that way?

To solve this problem, many different methods of bed-making have been tried on private and hospital patients. The sleeping bag seems the best solution. The one in use at present is a piece of cloth folded to open in the front, sewed across the top over each shoulder, leaving 4 inches (10.1 cm.) for the neck. Tapes on the corners tie to the crib rods. The width of the bag is that of the crib. It is somewhat longer than the infant. The material is sheeting, Canton flannel, French flannel or light blanketing, depending on the season. The bag is pinned down the front; if the baby tries to get out, the edges can be folded to make a tight joint.

The baby wears the bag day and night up to 4 months of age, when the use of the hands begins, and after this for his nap and at night up to 2 or 3 years of age. He is free to kick and move his arms about in the bag. He can be put in either the prone or the supine position and learns to turn over in it at will. The diaper can be changed without removing the bag, and he can be fed in it. The bag keeps him from scratching his face, prevents thumb-sucking and kicking off the bedding. Blankets may be put on over it and will stay on. The bag may be used in place of a dress, the infant wearing only a diaper and shirt under it; in very hot weather even the shirt may be omitted. The baby becomes accustomed to sleeping with his shoulders covered and will remain covered when he is old enough to sleep without the bag.

The diaper is another great problem of infant care. The old triangular diaper is more easily applied than the square one recently much in favor. It stays in place better, requires fewer pins and is somewhat more efficient in catching the stools. The square diaper is apt to be too loose and to cover too much of the abdomen; thus more of the baby and his clothes are wet than necessary.

The wet diaper wets clothing and bedding unless covered by waterproof material. Physicians and nurses have frowned on this practice but mothers continue to use rubber or oiled cloth to keep the urine in the diaper. The main objection to a diaper covering has been that it causes irritation of the buttocks. This is not true if the diaper is changed as often as necessary. Red buttocks are due to irritating stools or urine and are just as frequent without the waterproof sheeting as with it. A trial of twenty-five years in private practice and of eight or ten years in the hospital has definitely proved this point. A good waterproof material is an oiled muslin sold under the name of "Stork Sheeting." This is bought by the yard, cut to a triangle and pinned loosely over the diaper. The bed, undershirt and sleeping bag are kept dry. The baby is cleaner to examine, requires much less nursing care, is more comfortable and is less liable to chilling and infection than when lying in a completely wet bed.

A recent test, lasting one week, was made in a ward on six babies with sheeting and six without it. At the end of the week the babies without sheeting had used about four hundred more pieces of laundry, roughly ten more pieces per baby per day. This saving in laundry more than pays for the sheeting. The extra time of nurses required for frequent changing of the entire bed is wasted time. Careful records of the condition of the buttocks confirmed former observations that the buttocks were red only when the stools were irritating.

The sleeping bag and waterproof sheeting are valuable items in the baby's clothing.

Sixth Session

Morning, June 19

ENCEPHALOGRAPHY IN CASES WITH FIXED LESIONS OF THE BRAIN. DR. BRONSON CROTHERS, DR. E. C. VOGT (by invitation) and DR. R. C. ELEY (by invitation).

This article appears in the August issue, p. 227.

DISCUSSION

DR. L. R. DEBUYS: I should like to have Dr. Crothers describe the technic of injecting the air, and the amount of fluid withdrawn and air injected.

DR. IRVINE MCQUARRIE: I think that both ethically and scientifically this study is not only justifiable but commendable. The feature that interested me was the possibility of learning something more about cases of epilepsy, particularly to distinguish those with tremendous organic change from the other group. I should not wish to spend much of my time making careful chemical studies on such a group of patients as Dr. Crothers described.

How may one know what the normal appearance is in infants with this condition? Has Dr. Crothers studied the same cases months apart, or does he plan to follow them, making encephalograms from time to time, and thereby to use the method for studying progress and correlating changes with the mental development?

DR. CHARLES G. KERLEY: I feel that this is a most useful demonstration, particularly from the economic and broad humanitarian standpoint. We all have these hopeless cases that pass from the pediatrician to the neurologist and from the neurologist to the pediatrician. All know that they are absolutely hopeless but no one can demonstrate it to the parents' satisfaction. The parents become desperate and consult all sorts of charlatans and practitioners of the irregular sort who promise cure with the result that the afflicted family spends a vast amount of time and money to no purpose. If by some means it is demonstrated definitely that a cure is impossible the situation will be accepted and the child placed where he belongs, among the permanently defective.

DR. BENJAMIN KRAMER: Encephalography apparently has been used much more extensively in Europe than in this country, especially for children.

About a year before the present meeting, Dr. Bogin and Dr. Holzsager, in my clinic, began a study of this method and its value in diagnosis, prognosis and treatment. We did not have as large a series as Dr. Crothers, but we had a considerable variety of cases. Fluoroscopy, as a preliminary to roentgen examination of the head, was found to be valuable. Under the fluoroscope, it is possible to change the position of the child and to watch the fluid traveling from one ventricle to the other or from one part of the ventricular system to the other and to tell immediately whether air has entered the ventricles at all, or whether enough air has been introduced to visualize adequately the ventricle as well as the subarachnoid space.

We have tried to measure the pressure during the injection, but have found this to be unnecessary; if one is careful to inject several cubic centimeters less air than fluid removed, by removing small amounts of fluid at a time and replacing it by somewhat lesser amounts of air until enough fluid has been removed there is slight danger of increasing the pressure in the subarachnoid space. As the air goes in, alterations in pulse and respiration are observed which occasionally may give rise to anxiety. We have had no fatalities that could reasonably be ascribed to the procedure. There is usually a moderate febrile reaction that lasts for several days. As a rule, younger children tolerate the procedure better than older ones. Patients with spastic cerebral diplegia may present an aggravation of symptoms for several days. The reactions in the spinal fluid are severe. At one time, we found a cell count as high as 8,000. The reaction is usually over within two or three days. If one does not attempt to replace all the fluid the reactions are much less severe. In one instance, we were unable to remove enough fluid or inject enough air to visualize either the ventricles or the cortical subarachnoid space. After the intravenous injection of hypertonic dextrose and the intramuscular injection of a small dose of magnesium sulphate this difficulty was overcome. The spaces were very clearly and adequately visualized.

As a rule, the air disappears in from forty-eight to seventy-two hours. Sometimes it may remain for longer time. There is no doubt that this method visualizes what in many instances can only be suspected, particularly in cases of dilatation of the ventricles with microcephaly or with normal-sized skulls, porencephaly, etc.

In the course of treatment of meningococcus meningitis, with beginning choking of the disks and rather severe headache, it is sometimes gratifying to be able to demonstrate that there is no block, as shown by the fact that air passes readily through the aqueduct into the ventricles.

In one instance, we thought that the administration of air caused a breaking up of adhesions, because the first fluid was clear. Later on, the fluid was more cloudy and there was a striking improvement in the condition of the patient following the procedure.

In Europe the injection of air has been used in the treatment for meningococcus meningitis in addition to the antimeningococcus serum, and in some clinics is used in young infants in place of antimeningococcus serum with rather striking benefit.

In a child, aged 7 months, who had had signs of meningitis for only a few days and who was subsequently found to have tuberculous meningitis we were able to demonstrate a definite dilatation of the ventricles. There was nothing to justify the assumption of the existence of this condition before the meningitis developed. To my knowledge, this is one of the few instances in which internal hydrocephalus was demonstrated during life in a patient with tuberculous meningitis.

Dr. Henry F. Helmholz: I have been called on almost daily to meet the situations described, and I want to call attention to one important fact that I do not believe can be emphasized too much. There are a number of near-brain surgeons in the country who feel that such pictures as these are definite evidence of increased intracranial pressure and justify a decompression, and who regularly operate on these patients. I am sure that if they saw these pictures they would

be convinced that they were fully justified in their operative procedure. The point, however, is that this is a secondary manifestation due to atrophy of the brain and not to primary pressure with secondary atrophy of the brain.

The other point that I want to stress is the matter of family relationship in cases of this kind. It seems to me that it is one's duty to see that the other children in the family are not neglected and that family life is not destroyed because the mother and father are taking a child of this type all over the country.

Dr. JOSEPH BRENNEMANN: Dr. Crothers has asked for a frank expression as to the ethical justification for a procedure of this sort in so large a series. I have been much interested in Dr. Crothers' work ever since he first started intensively in this peculiarly dark domain about which so little is known. I think that anything that would clarify the situation would be much welcomed.

I do not think that the question of whether the procedure was justifiable or not would enter into the mind of any one, except the surgeon who uses it. That simply shows how conscientious he is about it. Not only is it justifiable, but it ought to be done even if it leads to nothing more than clarifying our minds and avoiding the situation of which Dr. Helmholz just spoke.

One has to think, too, of another side. These are desperate propositions. People are willing to take any chance. I am sure that in many cases, after a procedure of this sort, the parents are ultimately disappointed that the mortality has been as low as it has. Death is preferable to the condition that exists in most of these cases, from the standpoint not only of the child or the parents, but also of the other children in the family, which is a tremendous factor.

I hope that Dr. Crothers will keep on doing this sort of thing and with a clear conscience.

Dr. CROTHERS: I did not enter much into the question of technic, but it is simple. In the first place, we do not believe that one needs to put in two needles. If two needles are inserted, the chance of extra bleeding is doubled. We insert a single needle, into the lumbar space, withdraw from 4 to 6 cc. of fluid, look in the water manometer, the type devised by Dr. Ayers, which is simply a standpipe manometer, and then put 5 cc. of air in the glass syringe. The head is moved back and forth from side to side. The amount of air varies enormously; sometimes 20 cc. of air will be all that one can get in. Sometimes as much as 200 cc. can be injected in children that are not obviously hydrocephalic. In such children the excess is carried by atrophy.

We use a single needle in the lumbar subarachnoid space, withdraw fluid in 5 cc. amounts and replace it with air by a syringe. A three-way stopcock is connected with a standpipe manometer. Thus, we control a volume by volume replacement by pressure readings.

The amount of air introduced varies from 30 to almost 200 cc. even when no external evidence of hydrocephalus is noted. We are not convinced that small variations of the amount of air in the subarachnoid spaces are conclusive.

In regard to Dr. Kramer's suggestion of fluoroscopy there is this to be said. The exposure necessary to assure good right and left lateral stereoscopic films and anteroposterior and postero-anterior flat films is considerable. For our purposes in the cases under review we prefer the films to the fluoroscopic evidence and hesitate to subject the child to both.

I imagine that the emptying of all spaces is followed by a more severe reaction than is partial emptying. It seems clear, however, that a consistent technic is desirable.

Dr. Helmholz' suggestion that a surgical procedure might be precipitated by the discovery of a large ventricle is interesting. The only answer is that the solution of a problem of this sort should not be undertaken by surgeons unless one is sure of the difference between neoplasm and atrophy. It seems to me that a relatively simple conception of the dynamics of the situation ought to be enough to repel the over-eager surgeon.

We have not felt as enthusiastic as Pancoast, Fay and others, but have found changes in the subarachnoid space. The presence of more or less small amounts of air in the frontal subarachnoid spaces has not seemed advisable. We have not felt justified in exposing a child of theoretically entirely normal intelligence and competence in every way to this procedure. One cannot take a dozen children and make controls of them. There are a number of children who have no motor defects indicative of a large deficiency of brain tissue, in whom normal sized ventricles and normal appearing subarachnoid spaces exist. Occasionally convulsions are caused by small lesions. We have seen enough cases to know about what the normal appearance is. The suggestion of repeating the ventriculogram, carrying out Dr. Kramer's suggestion of fluoroscopy, is interesting.

Dr. Vogt, who has made all the roentgenograms in the cases described, is worried about the length of time it takes to make two lateral anteroposterior and postero-anterior films. He feels that further exposure than that necessary for an anteroposterior film, particularly if there is going to be a control, may harm young children. It seems to me that this fear is reasonable. I should just want to take the best advice I could get as to the relative merits of fluoroscopy and straight pictures, in connection with how much actual exposure the child was receiving.

We have cut down the number of roentgenograms as much as possible. On children in whom we expect to make an encephalogram we do not take a preliminary plate of the skull first. Neither do we make a preliminary fluoroscopic examination. We have not felt justified in the use of fluoroscopy on a wide scale or of many repeated roentgenograms. I think, however, that it is a perfectly obvious method which adds to one's information.

The question that Dr. Kramer raised about the severity of the reaction being increased when the fluid was all taken out is interesting, because it explains a great many of the discrepancies between different writers. Any one who has investigated the recent literature on this subject knows that some writers pay almost no attention to ventricles and others none to the subarachnoid space. I do not think that there is any question but that the method of spinal injection is better than the direct ventricular injection. In the direct injection one learns nothing about the subarachnoid space. My feeling would be to develop some technic, which would always be the same. If, on the basis of fluoroscopy, etc., Dr. Kramer wants to stop short of emptying the supraspinal system, he will have his own series of pictures. On the other hand, some use jugular compression to remedy the rest, or make the injection of fluid of which Dr. Kramer spoke. It does not make a great deal of difference whether one draws the fluid out by jugular compression or draws it in by giving hypertonic salts, etc. One merely must have some comparable technic. Unless the child begins to fail, we empty all that we can get, but we do not usually do jugular compression.

I have not gone into the therapeutic applications of this procedure. In an inflammatory block of any kind, I think that there is a fair chance of success if one dislocates pressure by the injection of air. I think that this is more sensible than to force fluid in, and certainly offers a chance. I did not go into the therapeutics of this thing, because I did not think that there should be a question of ethics. We have had several cases of epilepsy in which this method has revealed a lesion, and the attacks have stopped. It is easy to say that you should use it with the hope that it would control convulsions. I do not think that that is a good reason, but it is a fact that more good than harm seems to have followed the procedure therapeutically, except for the immediate reaction.

I think that Dr. Helmholz' point is well taken. If this were any lesser erudite assemblage, each film would result in an argument as to whether the large ventricle is sunk over to its own side of the head and is associated with subarachnoid enlargement. I think that it is clear that it would take a singularly unmedical mind and a singularly daring temperament to interfere on the basis of shrinkage of this sort. I think the whole question really comes down to the fact that, as far as the group described is concerned, here is a method that resolves many

doubts in a field that has been full of them. I do not think that any one who handles neurologic material has to master this method. There are many times when it is a matter of life and death to know where the circulation of the spinal fluid is. Sometimes one can tackle it with difficulty with four or five needles and sometimes with one needle and have a syringe full of air.

SYMPTOMATOLOGY CONNECTED WITH DEVELOPMENTAL PERITONEAL BANDS IN CHILDREN. DR. ROYAL STORRS HAYNES.

Children, as well as adults, may suffer from ill health owing to the effect of anomalous peritoneal bands, which deform the intestine and interfere with its function. It often requires long acquaintance with the child before such a condition is suspected because, although abdominal pain is frequent, it is not always present. In the histories of such children, vomiting in infancy and vomiting attacks from 3 to 5 years of age are frequent. These children eat poorly and are easily satisfied; if they eat fairly well, they are liable to vomit, with or without discomfort; they often vomit food taken twelve or more hours previously and certain foods are poorly borne. With their attacks they may have diarrhea, but they are more likely to be sluggish and even really constipated. They are subject to abdominal distention, the type of which may aid in diagnosis.

If they have discomfort it is liable to be in either the epigastrium or the right lower quadrant of the abdomen. In the former locality it may be over the first part of the duodenum or over the angle of Treitz. The discomfort may vary in degree from heaviness to severe pain akin to that in acute intestinal obstruction. Position often relieves the high type. Often the lower type is confused with appendicitis and the appendix is properly removed but without relief of symptoms.

Entirely without discomfort these children may suffer from interference with nutrition and from reflex disturbances; these occur also in cases in which there is discomfort. A characteristic sign is a grayish muddy pallor, not due to anemia. This may be the starting point for making a diagnosis. It disappears on surgical relief of the distortions. Besides constant pallor these children have moments of increased pallor at which times they may faint. This resembles the reflex shock of traction on the peritoneum; it may be confused with thymus disease. Growth is often interfered with. Postural difficulties are related to the presence of a peritoneal band both as aggravating cause and as effect.

Nervous manifestations are seen. Sadness, sensitiveness, anxiety and lack of gaiety or irritability and poor behavior are observed. Fatigue and lack of stamina are part of the picture.

Such symptoms may be relieved or removed by a proper regimen; surgical intervention often produces striking changes in the whole life and health of the child.

DISCUSSION

DR. CHARLES G. KERLEY: Dr. Haynes' contribution is particularly valuable in that he calls attention to the fact that chronic gastro-intestinal disturbances may be due to defective gastro-intestinal mechanics.

The child is usually assumed to be structurally normal; that this is an error I have emphasized in different contributions. Continued gastro-intestinal derangements under the right dietetic management call for serial roentgen studies of the gastro-intestinal mechanism.

L. R. DEBUYS: The cases that Dr. Haynes has so clearly described should certainly be recognized, because they cause a great deal of concern. What I wish to mention is the recognition of some of those defects in the early period of infancy, particularly in the first few months. The condition must be differentiated from the pyloric obstructions, both spasm and hypertrophic stenosis.

I have in mind a case that illustrates this. A child, 8 months of age, weighed about as much as the average infant aged 12 weeks. There was projectile vomiting, but no peristaltic waves could be demonstrated. The stools were small and well digested. On one or two occasions there had been diarrhea. There was a

mixture of the symptoms of spasm and of hypertrophic stenosis. The child did not thrive, even after the nutrition had been adjusted, as evidenced by perfectly digested stools.

On gastro-intestinal examination it was found that the stomach was fixed high up under the diaphragm. No air ball was demonstrable. We thought of the possibility of there being some diaphragmatic anomaly or possibly some adhesions holding the stomach in that position. There was some residue in the stomach after twenty-four hours' observation. It was necessary to make some opening for the food to enter the intestines so as to allow the patient sufficient nourishment for it to thrive. An operation was performed and a congenital defect was found to be present.

DR. DEWITT H. SHERMAN: Dr. Haynes referred mostly to older children. I think that the condition occurs in infants and often is not considered.

One of my earliest mistakes in the diagnosis of hypertrophic pyloric stenosis in a new-born infant was revealed at operation; there was a matting together of folds of the duodenum by peritoneal bands. In the few cases of this kind that have come under my observation I have found a history of an infection in the mother during pregnancy, such as influenza.

If crying is a prominent symptom of this condition and if all the other signs and symptoms of indigestion, either gastric or intestinal, can be eliminated, this condition of peritoneal bands should be thought of, regardless of the age of the patient.

In the new-born infant the maternal history is most important and indicative. In older children, in whom the condition comes on gradually, the history may or may not be suggestive.

DR. JOSEPH BRENNEMANN: I think that the interesting thing about this paper is the enormously large number of cases that Dr. Haynes has seen. We have all seen a few of them, but the large number that he has described is surprising.

DR. HAYNES: Having only fifteen minutes, I had to leave out many things that I should like to have said. I wanted others to have the experience that I have had in the last few years in suspecting and confirming my roentgen observations and possibly my surgical interventions in these cases which sometimes are not recognized.

If a child with symptoms suggestive of obstruction from developmental causes is examined roentgenologically the following method may be used: The roentgenologist makes a fluoroscopic examination. After a few minutes, he makes a roentgenogram; twenty or thirty minutes later, he takes another picture. If the whole series is taken in that way it is of little value. On the other hand, when the roentgenologist examines fluoroscopically what he sees, beginning immediately with the swallowing of the barium and taking perhaps twenty pictures during the first hour, he obtains pictures that the other method will not yield. Sometimes there is a delay of four hours before a second picture is taken. I have had to diagnose a case of duodenal obstruction because of the residue in the stomach, four hours after the first picture was taken. Likewise, the examination of the gastro-intestinal tract by enema is incomplete, yet that sometimes satisfies the physician in charge. In one case referred to me for a different condition the roentgenogram showed definite evidence of trouble around the duodenum. There was close association of hepatic flexure with the stomach; in a position where it should be attached to the stomach and duodenum, the pulling of the hepatic flexure to the right was suggestive. Many roentgenograms should be taken; they should be begun at once and taken together with fluoroscopy.

The second handicap is the attitude of the surgeon. A few surgeons are also physiologists. A great many of them say that the condition is there but that it does not cause any trouble. Yet, the surgeon is not altogether to blame. Granted that one has made a diagnosis and established it by roentgen observation, if the abdomen is opened by a vertical incision, it is almost impossible for one to reach

the area and see the anomaly. The horizontal incision gives a better exposure. Even if the bands are known to be there and horizontal incision is made, it is often difficult to see them on the ascending colon; it is only when one picks up what is apparently tissue over the ascending colon, cuts through it and finds another normal layer that one realizes that there is a band.

What Dr. Kerley has to say, of course, fits in perfectly with the attitude that I have toward the situation and the possibility of the bands causing acute intestinal obstruction. For instance, a boy ate canned pineapple and began having attacks of acute intestinal obstruction which kept us anxious for several days. Several months later, in school, he had a similar experience with pineapple. It was not until we realized that there were no enzymes to digest the cellulose that the possibility of obstruction was considered. He ate a sandwich made of gristly lamb and had another attack. Roentgenograms showed distinct narrowing of the duodenum. The pineapple or gristly meat blocked the intestine and brought about a serious condition.

I am much interested in Dr. DeBuys' case. There are few cases reported in children of that age. I have not seen cases in children younger than 4 years. There is no reason why symptoms should not develop in infancy. The more such cases are looked for the more they will be found. It is distinctly difficult to operate on them at the time that one is looking for hypertrophic stenosis. It requires a courageous person. I was hoping that Dr. Wilcox could take up this procedure at the Babies' Hospital. It is interesting in connection with the idea of peritonitis.

In studies made in 1903 by an English anatomist, practically all the bands were found in a series of fetuses from early age up to the time of birth. One thing of interest was in connection with the pericolic membrane, which often looks like a piece of omentum attached to the lateral wall. In a number of early fetuses he found that the omentum is attached all the way down the ascending colon, as it is normally in the adult monkey. If one considers that idea of development and comparative anatomy in the location of these pericolic membranes, in their resemblance to the omentum, an excellent theory may be brought out as to the manner in which these bands develop.

I am more interested in the nutritional side. It is easy to search for the cause of pain, but a great many children and adults with this condition have no pain. I observed a brother and sister with these bands who were operated on, in whom the symptoms developed only in adult life.

I was particularly struck with the discussion on anomalies of the urinary tract at a previous session. It was stated that a great many people have them, and that it is only when an infection or disturbance occurs that pyuria begins to develop. Likewise when these persons have a disease such as grip, the condition that they have had all their lives begins to cause symptoms. The greatest results are seen in the children who are pale, who lag behind their brothers and sisters and have a poor color, and for whom there is little to offer. A child whom I had watched from birth was operated on recently. It was only after a long time that I had made the correct diagnosis. The patient had no pain but had a poor color and nervous symptoms amounting almost to neurasthenia. Almost immediately after the operation she showed the natural spontaneous gaiety of childhood.

PERICARDITIS WITH EFFUSION. DR. LUCY PORTER SUTTON.

Moderate and large amounts of pericardial effusion produce characteristic pulmonary signs. Pins, in 1899, first called attention to them, but the fact has not received general recognition in spite of an extensive article by Curshmann in 1907 and a recent study by Connor.

When the pericardial sac is inflamed, as it is in rheumatic carditis, it may become greatly distended and hold a large amount of fluid. Contrary to early teaching, the heart because of its attachments cannot sink downward and back-

ward in the presence of an effusion, but remains close to the anterior wall of the chest. Both the left and the right pouches of the pericardium distend laterally and posteriorly when filled with fluid. For anatomic reasons the left pouch becomes more distended than the right. As the amount of fluid increases, the pericardium distends posteriorly until it comes in contact with the posterior wall of the chest. The lung is pushed upward and laterally. The signs thus produced are a rounded area of dulness to flatness on the left side below the scapula, with intense bronchial voice and breath sounds. Sometimes there is a similar but less extensive area on the right side. An area of resonance is found between the posterior area of dulness and the left border of cardiac dulness. The differential diagnosis involves chiefly pleural effusion which is a less common complication of rheumatic carditis.

During the past year at Bellevue Hospital eight children showing these signs were studied. In every case pleural effusion was excluded by roentgen and fluoroscopic examination. The pericardium was tapped posteriorly at about the center of the area of the most marked signs and fluid was obtained in every case. The signs described should therefore be considered characteristic of pericardial effusion. The posterior site for tapping the pericardium is the easiest, safest and most certain in obtaining fluid for diagnostic or therapeutic purposes.

Slides were shown demonstrating the anatomic position of the pericardium; abstracts of four cases were given and roentgenograms in all the eight patients who were tapped were shown.

DISCUSSION

DR. CHARLES HENDEE SMITH: It seems to me that this is a distinct addition to the knowledge about heart disease and has gone far to clear up the puzzling signs in the posterior part of the chest in the cases of acute carditis. No one who has examined children with heart disease has failed to observe these signs. For years, we have had spirited discussions at staff conferences as to the probable cause. The old idea was to attribute the bronchial breathing and dulness to the heart compressing the lung. The trouble was that the largest hearts failed to give these signs. We were therefore forced to make the diagnosis of encapsulated effusion behind the heart. If the child had an elevation of temperature, complicating pneumonia was suspected. Perhaps the single regular observation at autopsy in cases of fatal carditis is pulmonary infarction. The trouble is, however, that the infarcts occur in any part of the lung, whereas these signs are almost always at the base of the left lung, but are occasionally at the base of the right lung. It is easy to go back over old records and find many cases with diagrams corresponding closely to those which Dr. Sutton has shown that were diagnosed pneumonia or infarction.

The rapid development and rapid subsidence of fever in these cases is extremely interesting. I formerly thought that pericardial effusion developed slowly and took a long time to absorb; that it was a slow, tedious, chronic process. That was not true of many of the cases mentioned. There was a short period of fever, with acute fibrinous pericarditis, a free interval, and then a fever lasting four days, with the rapid development of physical signs in the lungs. The removal of a small amount of fluid for diagnostic purposes, which could not have influenced the course markedly, was often followed by rapid subsidence of the fever and physical signs.

At first, it seemed almost incredible that the pericardium could be stretched so rapidly as to impinge on the posterior wall of the chest, but there is little doubt that this is the case. The diagnosis of these signs is helped by careful mapping of the area over which they exist. The charts all show the area where the signs were present, the upper limit of which fell off abruptly, in contradistinction to the ordinary line of pleural effusion, which is always lower at the spine than it is at the posterior scapular line; when high in that line, it always falls off toward the axilla, which is the classic Ellis line. Careful mapping of the area of signs

on the chest has always shown this difference in pericardial effusion. That is an important diagnostic point. Often in private practice, cases of pericarditis are seen in which the patients are too ill to be taken to the hospital and in which it is not possible to have an adequate roentgenogram.

In a case of carditis the development of signs in the back should suggest effusions if the outline of the area is round or square without an ictus line. One is justified in tapping posteriorly. We have all been afraid of tapping the front of the chest, for many years. I am sure that the present study shows that our fears are perhaps justified because the heart is always held against the anterior wall of the chest. It is perfectly safe to make an incision posteriorly. The pericardial effusion must go under the hilus of the lung and push the lung up and laterally, not compressing it against the posterior wall of the chest.

FURTHER OBSERVATIONS ON THE USE OF VITAMIN B IN DIETS OF INFANTS. DR. B. R. HOOBLER.

The existence of at least two different factors in vitamin B has been proved, and evidence is rather conclusive for the existence of a third. An agreement to call the antineuritic, heat-labile fraction B and the more heat-stable, water-soluble, antipellagric factor G has been reached. The third factor appears to be water-soluble and heat-stable and is concerned with the nutritive utilization of food.

A number of foods have been evaluated as to their content of B and G. Wheat, brewers' yeast and lean pork are rich in vitamin B while bakers' yeast and fresh milk are richer in G.

Large amounts of the antineuritic factor for growing and for lactating animals are required. In lactation the increased requirement is necessitated since transfer of vitamin to the milk is not quantitative.

In addition to the work that has been done in the laboratories considerable clinical observation has been recorded. Five papers have appeared indicating the occurrence of clearcut cases of infantile beri-beri in several sections of the United States. These centers have been in South Carolina, Louisiana, Virginia, New York and the Canal Zone. Papers also have been published covering different phases of partial deficiency in the diets of infants indicating that the use of highly milled cereals with increasing quantities of carbohydrates is producing a diet low in vitamin B.

The original work contained in this paper was carried out on approximately 125 infants studied over a period of five months. The infants were all on whole milk dilutions with dextrimaltose no. 2 added in suitable quantities. From time to time additions of vitamin B in the form of wheat germ extract and yeast extract were made and the results noted. A series was given wheat germ extract only, and another yeast extract only, to compare the efficiency of these two substances. The accompanying tables show the results obtained.

TABLE 1.—*Total Average Monthly Growth of Infants Studied*

	Inches
Breast-fed infants	0.97
Controls fed dextrimaltose	0.818
Infants fed dextrimaltose and vitamin B	0.91

TABLE 2.—*Average Monthly Growth in Stem Length of Infants Studied*

	Inches
Breast-fed infants	0.675
Controls fed dextrimaltose	0.63
Infants fed dextrimaltose and vitamin B	0.735

TABLE 3.—*Average Daily Gain in Weight of Infants Studied*

	Oz.
Breast-fed controls	0.816
Controls fed dextrimaltose	0.801
Infants fed dextrimaltose and vitamin B additions	0.788

TABLE 4.—*Average Daily Gain in Weight of Infants Fed Wheat Germ and Yeast Extract*

	Oz.
Breast-fed infants	0.893
Infants fed dextrimaltose and extract of 0.5 Gm. brewers' yeast	0.850
Infants fed dextrimaltose and extract of 1 Gm. wheat germ	0.838
Infants fed dextrimaltose only	0.793

TABLE 5.—*Effect of Dextrimaltose with Vitamin B Additions on Spasticity*

	1st Mo.	2nd Mo.	3rd Mo.	4th Mo.	5th Mo.
Gloria B. on dextrimaltose and vitamin B	5	3	1	1	0
Douglas E. on dextrimaltose	4	3	2	1	0
Robert H. on breast milk and concentrated brewers' yeast	5	3	2	0	0

Table 1 shows the total average growth during a period of twenty-eight days. The breast-fed infants grew most; those fed dextrimaltose no. 2 and vitamin B additions showed slightly less growth while those given dextrimaltose no. 2 only showed considerably less.

Table 2 takes into account the growth in stem length. In measuring both total and stem length, the methods used at the Merrill Palmer School were employed. Infants fed dextrimaltose with vitamin B additions made the best showing, the breast-fed controls next and those fed dextrimaltose no. 2 the poorest.

The gains in weight shown in table 3 are practically the same on breast milk, dextrimaltose and dextrimaltose plus vitamin B additions of a combination of extract of wheat germ and yeast.

A study of fifty-seven infants during a period of two weeks was made in an attempt to determine which was the better, wheat germ or yeast extract (table 4). Again the variations in gain were so narrow that no definite conclusions could be drawn, but breast-fed controls showed the highest average daily gain, the infants fed yeast extract the next, those fed wheat germ the next and those fed dextrimaltose no. 2 the least.

Neither dextrimaltose no. 2 nor dextrimaltose no. 2 with vitamin B additions was able to clear up the spasticity (table 5). About twenty of the 125 infants studied showed varying degrees of stiffness. I believe this to be about the ratio found in the usual hospital ward devoted to feeding cases. It was evident that ten of these twenty infants required more vitamin B than was contained in the additions supplied. It has been my experience that the administration of brewers' yeast concentrate or powdered yeast is a more effective way of supplying the vitamin B complex; this is borne out by the observations of Bloxsom. It should be noted that one of the most marked instances of rigidity occurred in a breast-fed child. At the 1926 meeting of the Society, in collaboration with Macy and Outhouse I proved beyond question that human milk was relatively low in vitamin B content. Table 5 shows how rapidly the rigidity cleared up under brewers' yeast concentrate.

The conclusions reached were:

1. Wheat germ and yeast, in the form of dried powdered watery extracts, when added in the proportions of 1 Gm. of wheat germ extract and 0.5 Gm. of yeast

extract to 1 ounce of dextrimaltose no. 2 and fed to infants caused no appreciable gain in weight over controls who were fed on similar formulas without vitamin B additions.

2. Infants given vitamin B additions, as described, showed a greater growth in recumbent and stem length than controls not given the vitamin B additions.

3. About one out of six of the infants studied showed symptoms of rigidity. This symptom disappeared in all but six of the cases, indicating that the quantity of vitamin B needed by infants differs greatly and that one should bear in mind that while the amount of vitamin B in the commercial carbohydrate preparations may be sufficient for certain infants, there are others who will require larger quantities.

DISCUSSION

DR. F. F. TISDALL: Dr. Hoobler mentioned some interesting points that remind me of some of our work. In our work on birds we found that they required practically no vitamin B 2. In Canada, the vitamins are called B 1 and B 2, while in the United States, they are called B and G. It seems to us easier to keep the vitamin B complex together. We give yeast on the basis of vitamin B content. One of the widely advertised yeasts contains the least vitamin B 1 of all the yeasts that we tested. As Dr. Hoobler stated, brewers' yeast is much more potent in B 1 than is bakers' yeast.

What is the relation between the type of infant to which Dr. Hoobler referred and the one called hypertonic, the infant that is sometimes suspected of pyloric stenosis and that responds in a remarkable way to the administration of atropine? Is the hypertonic infant being confused with those showing vitamin B deficiency, or are we dealing with two separate conditions?

DR. HOOBLER: Any type of deficiency that will produce more or less starvation, such as in this case of pyloric spasm or pyloric stenosis, and particularly in hypertonic children, will also lead to deficiencies of all the vitamins. However, the children I described presented purely nutritional problems; there was no vomiting, diarrhea or constipation. They presented what might be called the average feeding case. I am sure that all the members present could pick out this type of child in the wards of their respective hospitals.

I started to work on this smaller amount of vitamin B, thinking that perhaps it would suffice. I do not believe that the quantity used is sufficient to relieve the rigidity or even to produce the best type of growth, although there was evident growth in stature above the controls. Nevertheless, I think that one should be cautious about accepting the commercial preparations in toto and think that they supply all the children's needs. One should be on the watch constantly to see whether the symptoms are being cleared up. It should not take three, four and five months to clear up the spasticity in these children when, on a concentrated vitamin B preparation, it can be cleared up in a few weeks. I have seen remarkable clearing in a week and sometimes in two weeks. At the end of a month it should be cleared up. The children who still show spasticity at the end of this study are to be given the more powerful forms of vitamin B. The results will be reported later.

THE DIAGNOSIS OF EARLY RHEUMATIC HEART DISEASE IN CHILDREN. DR. MAX SEHAM.

My purpose in this paper is threefold: (1) an attempt to classify all of the children admitted into the Minneapolis Lymanhurst Heart Clinic for children from 1923 to 1930 (809 cases); (2) a rough scheme for the differential diagnosis between conditions that simulate organic heart disease and true rheumatic heart disease; (3) a statistical analysis of all the material with especial reference to the five methods of diagnosis, namely, (*a*) etiologic, (*b*) clinical or structural, (*c*) functional, (*d*) roentgenologic and (*e*) electrocardiographic.

Slides were presented showing: (1) a classification of 809 cases; (2) the differential diagnosis of (*a*) no heart disease, (*b*) rheumatism and murmur (unproved), (*c*) early mitral disease and (*d*) congenital heart disease (patencies); (3) the etiology of rheumatic heart disease; (4) the percentage relation between the abnormal roentgenogram and the thoracic heart index in heart disease; (5) the relation between the roetgenogram and the thoracic heart index; (6) the relation between the thoracic heart index and the functional diagnosis; (7) the relation between the roentgenogram and the functional diagnosis; (8) the effect of maximum dumb-bell exercises on the blood pressure; (9) a comparison of the blood pressure and pulse rate between the normal condition and heart disease; (10) the anatomic relationship between the left auricle and the esophagus; (11) a right lateral view of an esophogram; (12) the percentage relation between the esophogram and the roentgen and clinical diagnosis; (13) the electrocardiogram in rheumatic heart disease; (14) an electrocardiogram, showing the absent iso-electric period.

The data presented justify the following conclusions: 1. For early diagnosis of rheumatic heart disease, all available methods are necessary, namely, (*a*) etiologic, (*b*) clinical, (*c*) functional, (*d*) roentgenologic and (*e*) electrocardiographic.

2. The problem of diagnosis revolves chiefly around those cases with (*a*) systolic murmur, with or without circulatory signs and symptoms, (*b*) rheumatism and a systolic murmur that escapes a valvulitis, (*c*) those with rheumatism and systolic murmur in which chronic endocarditis ultimately develops and (*d*) congenital heart disease, especially patencies.

3. Rheumatism alone causes 39.3 per cent of cases of rheumatic heart disease. Rheumatism in combination causes 83.1 per cent.

4. Growing pains alone are responsible for 2.3 per cent.

5. The electrocardiogram, roentgenogram and esophogram are of great help in differential diagnosis.

6. In the first contact 42 per cent of the cases diagnosed early mitral disease show abnormal roentgenograms, and in those diagnosed "all others" 84 per cent were abnormal.

7. The esophogram reveals dilatation and hypertrophy of the left auricle. This does not appear in congenital or miscellaneous heart disease, or in normal children.

8. The absent iso-electric periods in lead to the delayed P. r. interval are indications of active rheumatic infection. They do not occur when there has been no rheumatism.

This study was made possible by a grant from the University of Minnesota Medical School. Dr. M. Shapiro made the study of the electrocardiograms, and Drs. E. Hilbert and Grete Seaham helped in the statistical analysis.

Seventh Session

Afternoon, June 19

STUDIES ON A CASE OF SICKLE CELL ANEMIA. DR. JESSIE BOYD SCRIVER (by invitation) and DR. T. R. WAUGH (by invitation).

A case of sickle cell anemia is reported from a Canadian clinic. L. H., a Negro child, was admitted complaining of cough, night sweats, pains in the legs and joints, occasional abdominal pain, poor appetite and increasing fatigue. The physical observations and blood picture were typical of sickle cell anemia.

To determine the correlation between gaseous changes in the blood and the phenomenon of sickling, blood was obtained from the antecubital vein; it was first taken without the application of an esmarch. This showed from 15 to 20 per cent sickle cells in wet sealed preparations. Blood taken after marked stasis had been established by means of a tight esmarch showed 95 per cent sickle cells

Blood taken after friction had been applied and the arm immersed in hot water to promote maximum oxygenation showed from 5 to 10 per cent sickle cells.

The carbon dioxide and oxygen contents were determined on these samples; an oxygen dissociation curve was also obtained on the blood. The oxygen dissociation curve presented a shift to the right as is seen in severe anemia, but the type of curve was essentially normal.

The curve was plotted to show the relationship of the oxygen pressure, in millimeters of mercury, to the percentage of sickle cells found in the patient's blood at the different percentages of oxygen saturation incident with anoxemia and maximum oxygenation; a definite change was seen with increased sickling around a pressure of 40 mm. of mercury. This corroborates the in vitro observations of Hahn who showed sickling to take place when the partial oxygen pressure fell below 45 mm. of mercury.

Thus it would appear that the phenomenon of sickling is dependent on varying partial oxygen pressure of the blood and is due to an inherited property of the red cells which probably follows the mendelian law and is peculiar to the Negro race.

DISCUSSION

DR. THOMAS B. COOLEY: I should like to ask Dr. Scriver whether she was able to repeat Hahn's results in his gas chamber experiments. We have never been able to reproduce these results nor have some other workers; on the other hand, some workers have done so without any trouble. I have wondered whether bloods might differ in this respect. I think that Dr. Scriver is to be congratulated on having succeeded in demonstrating the presence of sickle cells in the circulating blood under conditions of anoxemia. I think that she is the first to have done this.

DR. SCRIVER: Dr. Waugh performed the morphologic work. We tried to adjust a gas chamber similar to Dr. Hahn's. We were not successful with our results, but thought that perhaps we were not as careful with our preparation. We were not able to duplicate the test tube results, but did not persist long with them. We were interested in whether we could do this in vivo experiments.

ACTIVE IMMUNIZATION AGAINST POLIOMYELITIS IN MONKEYS. DR. A. GOLDBLOOM, DR. M. BRODIE and DR. W. MOFFATT.

The first attempts to produce active immunity against poliomyelitis in monkeys were made in 1910 by Flexner and Lewis. They obtained some immunity by using repeated small doses (0.05 Gm. of a 5 per cent suspension of spinal cord). In the same year, the same observers showed that the use of a mixture of virus suspension and immune serum did not confer any immunity in these animals, while Roma and Joseph claimed success by this method. Other observers, such as Landstein and Levaditi (1910), Kraus (1911), Zappert (1911), Romer (1912), and more recently, Aycock and Kagan (1918 and 1924), studied various methods of immunization with indifferent results. Aycock and Kagan finally demonstrated that more consistent results could be obtained by using the intracutaneous method, making from twenty to forty punctures over the shaved skin of the abdomen and thorax. Rhodes, in 1930, has shown that immunity could be produced with one massive dose given intracutaneously. Criteria of immunity were either the ability of the animals to resist intracerebral inoculations of active virus or the biologic test of the ability of the serum of the animal to neutralize active virus injected intracerebrally into another animal.

At first, we attempted to repeat the work of Roma and Joseph, who claimed to have produced immunity by using mixtures of virus and immune serum. Five animals were given mixtures that had been incubated for two hours at 37° C., twice weekly for three weeks. Two of the animals died of miliary tuberculosis in the course of the experiment; the remaining three, after an interval of four weeks, did not resist intracerebral injections of 0.1 cc. of a 5 per cent virus suspension. The results therefore agree with those of Flexner and Lewis, who could not produce any immunity by this method.

Five animals were used in the next experiment. In view of the fact that attenuation of the virus outside the body of the animal, or its alteration in any way, invariably destroyed its antigenic powers, it was thought advisable to attempt the production of immunity by the use of those portions of the nervous system of a monkey which do not contain great amounts of virus. Virus is present in largest amounts in the spinal cord, medulla and site of inoculation in animals that die of poliomyelitis. Doses as small as 0.1 Gm. of a 5 per cent suspension, which represents only 5 mg. of nervous tissue, are sufficient to produce fatal poliomyelitis within six days following intracerebral injection. We wished to determine the antigenic effect of brain tissue that would not produce poliomyelitis when injected intracerebrally.

A slight modification of the technic was used with each animal. One animal was given 8 cc. of a 5 per cent suspension from brain tissue intracutaneously, and at the same time, and in another part of the body, 8 cc. of immune serum intracutaneously. Nine days later, the dose of brain suspension was repeated, but not the serum.

Another animal was given 5 cc. of the suspension intracutaneously and 5 cc. of the serum intramuscularly, then in five days 15 cc. of the suspension and 8 cc. of the serum, and ten days later 10 cc. of the suspension alone; in all, 30 cc. of the virus and 13 cc. of the serum were given. A third animal received 10 cc. of brain suspension intracutaneously, followed in two days by 10 cc. of immune serum intramuscularly, and three days later by 10 cc. of brain suspension and 5 cc. of serum; that is, 20 cc. of brain suspension and 15 cc. of serum were given.

A fourth animal was given 6 cc. of suspension, followed two days later by 6 cc. of serum, three days later by 10 cc. of brain suspension, two days later by 5 cc. of serum and three days later by 20 cc. of the suspension and 18 cc. of serum.

The fifth monkey received 20 cc. of brain suspension intradermally, and two days later 12 cc. of serum.

The control animal was given 12 cc. of immune serum. After an interval of six weeks, serum was taken from all the experimental animals, and injected into six monkeys. Each experimental monkey received 0.2 cc. of brain suspension with 0.8 cc. of serum from each animal intracerebrally, and the control was given 0.2 cc. of the suspension. All the animals given the injection remained well at the end of ten days, proving that the brain suspension used in the immunity experiments did not contain sufficient virus to produce poliomyelitis. Serum from each monkey was again taken; and 0.8 cc. of serum from each animal was incubated with 0.2 cc. of active cord virus, and again injected intracerebrally into the same six animals.

The control animal and three of those tested succumbed to poliomyelitis, and two resisted intracerebral inoculation. The animals that succumbed were those tested with the blood serum from the first three cited, which received totals of 16, 20 and 30 cc. of suspension in two or three divided doses; the two animals that resisted were the ones that received serum from the animals given 30 cc. of brain suspension in three doses, and 20 cc. of the suspension in a single dose.

The conclusions reached were: 1. Brain tissue, in itself unable to produce poliomyelitis, can produce immunity. 2. Serum, mixed with virus, has an inhibitory action on antigenesis. 3. Serum is to be given only after virus has acted alone for one or two days. 4. A large single dose is preferable to small or repeated smaller doses.

The Treatment for Spina Bifida and Cranium Bifidum with Protrusion by Penfield's Method. Dr. William V. Cone.

The accepted treatment for spina bifida and cranium bifidum has been the excision of the protruding sac and plastic repair of the defect. The results of such a procedure have been unsatisfactory. The immediate operative mortality is said to be from 42 to 50 per cent. Late complications develop. Cutler summarized this treatment by saying that while modern surgical methods make amputation

of the protruding sac safe so far as meningitis is concerned, they may be justly accused of causing death by producing hydrocephalus.

In 1922, Penfield instituted a new method of treatment based on the preservation of the protruding sac. He had concluded from observations made at operation and from postmortem studies that the sacs were not mere safety valves preventing increased intracranial tension, but that they were true absorbing mechanisms. The results attained by the application of this hypothesis have been so satisfactory that the technic of the procedure and a summary of the cases operated on in Dr. Penfield's clinic during the past year are worthy of recording.

The method of treatment as used in this clinic differs from any that has been previously described in that the meningocele sac is preserved in its entirety.

The infant is placed on the operating table in such a position that a minimal loss of cerebrospinal fluid will take place when the sac is opened. Under very light ether anesthesia the skin over the sac is dissected free. This may be a

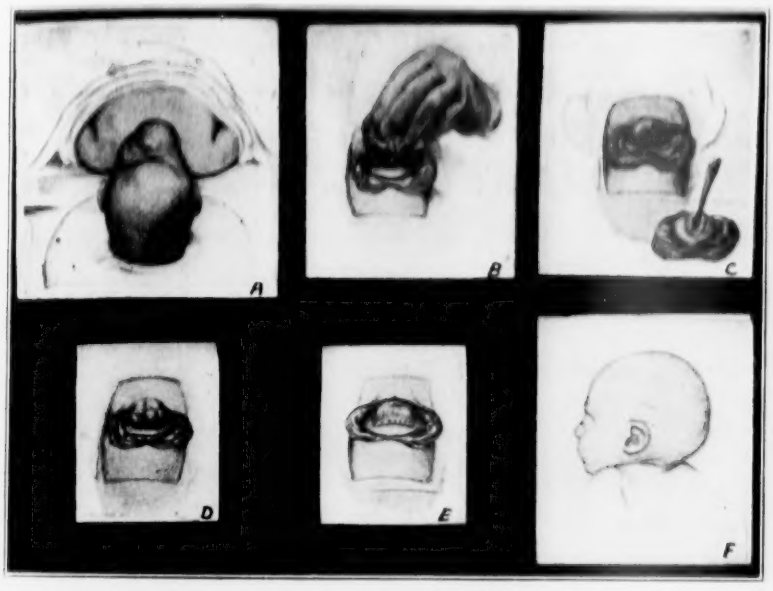


Fig. 1.—*A*, position at operation; *B*, sac completely dissected; *C*, sac widely opened and showing its content of cerebellum; *D*, sac sutured and folded in; *E*, sac and defect covered with fascia lata from father's thigh, and *F*, result.

tedious and delicate procedure in sacs of paper-like thinness. In the sacs with thicker walls a line of cleavage can quickly be obtained and the entire dissection rapidly carried out until the entire sac is exposed. An attempt is made to free the sac down to its point of origin, without rupturing it, for dissection of a collapsed sac is difficult. Not until the dissection is complete is the sac opened. With the opening of the sac and the escape of cerebrospinal fluid the contents of the sac can be determined.

Then the sac is folded in and covered by a pedicle flap of fascia or a sliding fascial transplant from the lumbar muscles. If the collapsed and folded sac and the defect are too large to be covered in this way, fascia lata from the father's thigh is used.

After operation the infant is kept face down with the head low until the wound is well healed. Then the head of the bed is elevated to reduce the intracranial pressure. If the fontanel remains tense, fluid intake is cut to a minimum by

concentration of the diet. For one year after operation the head of the bed is kept high, and the infant is never allowed to lie in a horizontal plane. Figures 1 and 2 illustrate the procedure used in two cases.

Since October, 1928, when the neurosurgical clinic was established in Montreal, Dr. Penfield and I have seen three encephalomeningoceles in the occipital region, one encephalomeningocele projecting through a defect in the ethmoid frontal and superior maxilla into the mouth, and fourteen myelomeningoceles. Opertaion has been performed in twelve of the eighteen cases, with but one death; that occurred in the case in which the sac appeared in the roof of the mouth.

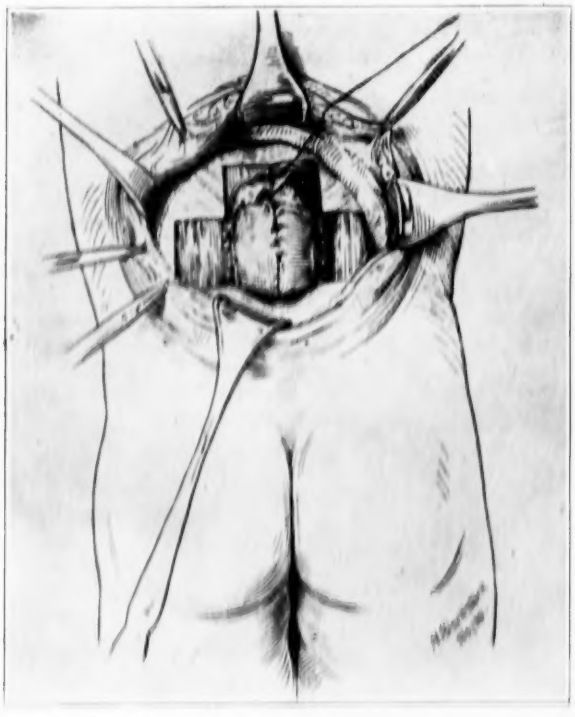


Fig. 2.—Fascial tent covering folded in meningocele sac.

Of the six infants that did not undergo operation, one showed a large hydrocephalus as well as spina bifida with protrusion, and surgical treatment was not advised. In the five remaining cases the parents decided against operation. Two of these five cases died of meningitis, one at 2 months and the other at 6 months of age. No data is available in the other three cases. These cases are cited to show that those in which operation was not performed were not selected cases. In the group subjected to operation, paralysis of variable degree was present in some instances.

Operations were performed within a day after birth if the skin over the sac was excoriated or so thin that rupture of the sac seemed imminent. Otherwise we waited until the infants were from 1 to 3 months of age, when the mothers could come to nurse them.

Hydrocephalus developed in none of the eleven infants operated on. Abnormal neurologic signs that were present before operation showed a tendency to diminish. At times a striking clearing of signs occurred.

Our enthusiasm for this new method of treatment can be better appreciated when the results of treatment by other methods are studied. With the present generally accepted surgical procedures it is advised that operation be postponed until after the first year of life. As so many of these infants die of complications within the first year of life, it is obvious that a method that makes early operation safe is of value.

In preserving the sac, not only are nervous structures, which may be contained in the sac wall, preserved but tissue that we feel absorbs cerebrospinal fluid is saved.

A Comparison of the Results Obtained in the Feeding of Infants According to Appetite on Sweet and Lactic Acid Milk Formula. Dr. H. P. Wright, Dr. A. K. Geddes and Dr. C. L. Vick.

Infants at the Montreal Foundling and Baby Hospital were fed according to appetite on 20 ounces (591.4 Gm.) of lactic acid whole milk with the addition of 2 ounces (85 Gm.) of 50 per cent corn syrup, and on 20 ounces of boiled whole milk with the addition of 2 ounces of 50 per cent corn syrup; the results were compared. The following procedure was adopted:

1. Irrespective of age, all infants were fed five times in twenty-four hours, each feeding lasting for twenty minutes. An ordinary anticolic nipple with a fairly large hole was used, so that one could reasonably assume that the infant received as much as he wanted during the twenty minutes.

2. When an infant took 32 ounces (946.3 Gm.) of this formula in twenty-four hours, cereals were offered twice daily and vegetable broth once, and the number of feedings were reduced to four. When the infant was receiving two platefuls of cereal daily, it was usually fed only three times in twenty-four hours.

3. Boiled water was offered to all infants between feedings.

4. Cod liver oil was administered to all infants from the day of admission and rapidly increased up to 1 teaspoonful twice a day. Orange juice was also given from admission and quickly increased to 1 tablespoonful daily.

The results obtained are shown in the accompanying table.

Results of Feeding on Lactic Acid and Sweet Milk

	Lactic Acid Milk	Boiled Milk
Number of cases	38	35
Average age on admission	54 days	37.9 days
Average number of days on feeding	116.4 days	87.8 days
Average age when cereal was commenced	4 months	3½ months
Youngest age when cereal was commenced	7 weeks	8 weeks
Average age when soup was commenced	4 months	3½ months
Average age on 4 feedings per day	6½ months	6 months
Youngest age on 4 feedings per day	3 months	3.5 months
Average age on 3 feedings per day	10.9 months	9.5 months
Youngest age on 3 feedings per day	8 months	9 months
Average number of stools per day	3.3 months	4.8 months
Average weekly gain in weight on lactic acid formula		5.8 oz.
Average weekly gain in weight on boiled milk formula		4.4 oz.
Average maximum weekly gain on lactic acid formula		14.8 oz.
Average maximum weekly gain on boiled milk formula		11.3 oz.
Greatest weekly gain on lactic acid formula		22 oz.
Greatest weekly gain on boiled milk formula		30 oz.
Average amount of lactic acid milk formula taken in 24 hours		30.6 oz.
Average amount of boiled milk formula taken in 24 hours		28.8 oz.
Maximum amount of lactic acid milk formula taken in 24 hours		52.5 oz.
Maximum amount of boiled milk formula taken in 24 hours		48 oz.
Maximum amount of individual feeding on lactic acid milk formula		16 oz.

Maximum amount of individual feeding on boiled milk formula..... 16.5 oz.
Average amount of individual feeding on lactic milk formula..... 6.1 oz.
Average amount of individual feeding on boiled milk formula..... 6 oz.

The conclusion arrived at was that the normal infant made a satisfactory gain in weight on either formula. The impression prevailed among those associated with the work that in the new-born infant mild digestive disturbances were more prone to occur in those fed unacidified milk; at present all very young infants receive an initial formula of 10 ounces (295.7 Gm.) of boiled whole milk, 1 ounce (29.5 Gm.) of corn syrup and 10 ounces of boiled water. Every day 1 ounce of water is withdrawn and 1 ounce of boiled milk added until a formula made up of 20 ounces of boiled whole milk with the addition of 50 per cent corn syrup is attained.

NURSERY SCHOOL STUDIES (LANTERN SLIDE DEMONSTRATION). DR. A. B. CHANDLER.

The results of the various studies are:

1. Food preferences of children of from 24 to 60 months of age, as shown by requests for second servings, in order of preference, were: bread and sandwiches, potatoes, meat, fish, eggs and tomatoes. Food left from the first serving in the order of occurrence included: pudding desserts, potatoes, egg, spinach, fruit desserts and meat.

2. The average eating time for the first course was fourteen minutes for children aged from 24 to 36 months and from 36 to 48 months and ten minutes for those from 48 to 60 months. For the second course the time was 6.4, 5.6 and 6 minutes respectively.

3. The time taken by the fastest and slowest eaters varied from nine to twenty-three minutes for the first course and from five to eleven minutes for the second.

4. The favorite dishes, as determined by the rapidity with which they were eaten were: fish, meat stew, egg and vegetable dinners; the favorite desserts were: chocolate blancmange, fruits and puddings.

5. A winter play suit made in one piece, of material to which snow does not stick, is windproof and light in weight, and allows for adequate activity so that the child can keep warm.

6. The favorite play materials of children aged 3 years were: Montessori cylinders, color-matching materials and large building-blocks. The average time of interest was eight minutes.

7. The favorite toys of children aged 4 years were Montessori frames and cylinders, metal insets for tracing and colored cubes. The average length of time spent with this was six minutes.

8. The attendance by age was slightly lower for children under 3 years of age. Variations of from 53 to 76 per cent were noted.

9. There was an average of 67 per cent attendance by months for one year. September, October, March and May showed attendance above the average and the other months below the average.

10. The incidence of colds for one year show peaks in November and April with a smaller one in January.

11. The sex incidence of colds showed nothing conclusive.

12. Absence records by months showed the relative importance of colds, illness and other factors.

13. Absence records by the day of the week showed that the largest number of absences occurred on Mondays.

14. Character rating charts can be made independently by different observers.

15. Height and weight charts were presented showing the different types of children.

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, March 18, 1930

A. H. PARMELEE, M.D., *President, in the Chair*

PRESENT STATUS OF THE PREVENTION AND TREATMENT OF SCARLET FEVER. DR. GEORGE F. DICK, by invitation.

DR. DICK gave a brief review of the report which was published in the AMERICAN JOURNAL OF DISEASES OF CHILDREN, **38**:905, 1929.

DISCUSSION

DR. MAURICE L. BLATT: I should like to ask Dr. Dick whose serum he is recommending. All of us are anxious to use the preparation that offers as much as we can anticipate, according to his statements, that such a serum does offer. All of us have had unfavorable experiences with reactions to scarlet fever serum. Some of the patients to whom I have given prophylactic injections were more sick than the ones who had scarlet fever, and because of that I felt that I had to apologize to the families to whom I had suggested antitoxin therapy. I have felt that not to give scarlet fever antitoxin to the child who had been exposed several days before the disease was recognized in his brother, was almost criminal, and to give the serum that one has had to use was almost criminal. I think that Dr. Dick should tell us what serum should be used.

DR. GEORGE DICK: The serums that are approved by the Scarlet Fever Committee are so marked on the outside where it can be readily seen.

I wish to point out that some reactions are seen from these serums. As I said, we got reactions recently in about 10.9 per cent of the cases. It is to be remembered that when these reactions occur a week or so after the injection they may cause considerable trouble, but one should compare a large series of cases in which serum is used with those in which it is not given. The discomfort and deafness may last for a few days, but it does not last long. Serum disease is a condition to be feared in the anaphylactic type of patient, and we do not believe in giving serum to all persons. If the patient has had hay-fever or serum has been given before, the procedure is that usually adopted in giving serum, tetanus antitoxin or what not. We do not like to give tetanus antitoxin to all persons, but would rather give it than risk tetanus. With one of the various serums that undergo concentration, there is about the same degree of reaction whether it is tetanus antitoxin, diphtheria antitoxin or any other antitoxin. The raw serums will give the worst reactions. In the war physicians did not like to give tetanus antitoxin to all the patients, but we did it, for the serum sickness would be slight compared with the complications and the double number of deaths that occurred without it.

DR. GEORGE E. BAXTER: Does Dr. Dick know yet how long immunization will last? Must the presence of the streptococcus be demonstrated in order to make a diagnosis of scarlet fever?

DR. G. F. DICK: I think that the diagnosis can be made easily without obtaining the streptococcus, and cultures are seldom depended on in making a diagnosis of scarlet fever. It occasionally happens that it is of importance, for some cases are difficult to diagnose. If there are not streptococci on repeated cultures from the throat, that evidence is as much against a diagnosis of scarlet fever as if in diphtheria no diphtheria bacilli are found. I had a case not long ago in which the disease occurred as primary pneumonia, and the only place in which hemolytic streptococci were found was in the sputum.

As to immunization, we do not know. We have had experience with the methods in use now for about four years. Immunization does not last that long in 100 per cent of the cases. Only about 95 per cent of the patients in our series are immunized at all, and between 5 and 10 per cent slip back and have to be tested again, but if they are immune at the end of a year they usually remain so. I think it is comparable to the immunization in diphtheria, excepting that with

the five doses now being sold by the leading manufacturers, a much higher percentage of children are immunized than with diphtheria toxin-antitoxin.

DR. CHARLES SCHOTT: When the antitoxin first came out I used it in all cases, but in the last two years I have not used it at all. In my small series of cases I had as many complications in cases when I used the serum as I had before I used it; in some of the patients whom I desensitized, the results were disastrous. My results have not been any worse without the use of the serum than with it. I may feel differently after hearing Dr. Dicks' paper.

DR. G. F. DICK: One can get very different impressions. I should like to know the percentages, whose serum was used, and when was it given?

DR. C. SCHOTT: I used Squibb's serum in every case, using it within twenty-four hours. I see perhaps from fifteen to twenty cases each year. I stopped using the prophylactic treatment on your advice about three years ago.

DR. G. F. DICK: It might easily be that you would get better results in 100 cases without the serum than with it. Statistics do not begin to be of value until one has a considerable number of cases. It may be that it is used in late cases. Often I find that physicians do not wish to use the serum unless they realize that the patient will die without it. How many deaths were there?

DR. C. SCHOTT: Three deaths, with as many complications as there could be.

DR. G. F. DICK: Three deaths in perhaps 100 cases with antitoxin treatment is high. I should like to call attention to three things concerning Dr. Schott's statement. First, he does not know accurately the total number of patients treated. Second, he had no controls. Third, and most important, the statement that in the cases in which antitoxin was used there were as many complications as there could be, if it means anything at all, means an inaccurate impression by a prejudiced observer, as it is almost impossible that in every case in which antitoxin was used every possible complication should result.

DR. H. F. IRISH: I wonder how many physicians have had any difficulty with immunization. A few years ago a child, aged 3, was given his third injection in my office. About one hour later I was called to see the child in what appeared to be an anaphylactic shock. He was cold, covered with sweat and he had vomited once. I gave $\frac{1}{200}$ grain (0.3 mg.) of atropine hydrochloride, applied external heat, and he came out of the condition in about an hour, with no further trouble. He had no reaction after the first two injections. Naturally, the parents were frightened, and the child did not receive any more antitoxin. I do not think that I struck a vein, but I may have. At any rate, the reaction was severe and alarming.

DR. G. F. DICK: I have had similar experiences. No matter what is used in the way of preventive injections, for diphtheria, typhoid or any other condition, similar reactions may be obtained. I have not seen any cases that were fatal. The trouble the physician has in carrying out the immunization depends on his own reaction to it. If one is frightened about it, the parents will be frightened also. If one assures them that the child will have no reaction, there will be disappointment. There will be reactions, some undesirable ones, with any efficient immunization agent about which I know anything. In the army men used to come in following immunization for typhoid with what was diagnosed as meningitis. These patients did not die, and they did not get typhoid fever. If the parents of children who are about to be immunized are warned that reactions will occur with nausea, vomiting and sometimes fever, but that the protection secured is worth much more than the price paid in reactions, no trouble will be experienced.

DR. JULIUS H. HESS: There has just been an epidemic of scarlet fever in the training school, and I will ask Dr. Sapoznik, who has charge of the work, to give you the results.

DR. H. I. SAPOZNIK: In the month of January, 1930, an epidemic of scarlet fever occurred at Michael Reese Hospital. Nineteen cases developed over a period of eight weeks, in eighteen nurses and one intern. During this epidemic, passive immunization was attempted with two different serums. The Dick test was given to 250 nurses; 101 gave positive results. Of that 101 reactions, 45 were positive

III, 26 positive II, and 30 positive I. Only those who had a positive III reaction to the Dick test were given prophylactic scarlet fever antitoxin.

Prophylactic antitoxin A, a 2 cc. vial, was given to eleven first year nurses. (This antitoxin was furnished for scientific purposes by the Connaught Laboratories.)

Prophylactic antitoxin B, a 10 cc. vial, was given to thirty-four nurses. (This antitoxin was manufactured by Squibb and Son, and was purchased by the hospital.)

Those nurses receiving antitoxin A showed no evidence of serum sickness at any time, while those nurses receiving antitoxin B showed a severe serum reaction in 82 per cent of the cases, and the symptomatology was intense. The striking symptoms in twenty eight cases were as follows: skin eruptions consisting of urticaria, erythema and scarlatiniform; polyarthritis with pain, tenderness and limitation of motion of all joints; enlargement of cervical lymph nodes; elevation of temperature to from 100 to 104 F. (for from two to five days); edema of the nephritic distribution type, and severe sore throats.

There was early menstruatoin in six cases, conjunctivitis in four, blurring vision in three, partial deafness in three and delirium and convulsive movements in two. There was a leukocytosis from 10,000 to 16,000 in sixteen cases. The urine showed an albuminuria varying from a trace to 4 plus, with white blood cells and red blood cells and casts, and in three cases double refraction of lipoids.

In three cases in which serum B was given, scarlet fever developed following the injection of the scarlet fever antitoxin in eight, twelve and fourteen days after the injection.

Serum Sickness from Scarlet Fever Antitoxin

Type of Serum	No. of Cases Given	Previous Immunization with Toxin-Antitoxin Mixture	No. of Reactions	Per Cent	Incubation Period	Symptomatology	Laboratory Observations	Cases Developing Scarlet Fever Following Serum Reaction
A	11	1	0	0	0	0	0	0
B	34	10	28	82	Immediate reactions 20 minutes (1 case) general urticaria with edema 2 hours (1 case) chills, fainting, general aches 24 hours (4 cases) 6 days (16 cases) 7-10 days (10 cases)	1. Urticaria (wheal formation) (a) Erythema (8 cases) (b) Scarlatine (30 cases) 2. Polyarthritis (100%) (a) Pain (b) Tender (c) Swelling (d) Redness (e) Limitation of motion 3. Enlargement of cervical lymph nodes (100%) 4. Fever (100 to 104 F., 2-5 days) 5. Edema (nephritic distribution, face and extremities, 100%) 6. Sore throats (severe; inflamed, edema (one; 100%) 7. Early menstruation (6 cases) 8. Conjunctivitis (4 cases) 9. Convulsive movements with delirium (2 cases, 3-4 hours) 10. Blurring of vision (4-6 days, 3 cases) 11. Partial deafness (4-6 days, 3 cases)	Blood Leukocytosis 10,000-16,000 (in 16 cases in which tests were done) Urinalysis (in 25 cases done) Specific gravity (1.010-1.030) Albumin Trace to 4+ Sugar, 0 Acetone (8 cases) Microscopic examination Abnormal Amount white blood cells (2-10 high power field) Red blood cells; hyaline and granular casts; 8 cases (1)Three cases with eczema had double refraction of lipoids	1. Serum on 2/14/30 Reaction in 2/17/30 Scarlet fever on 2/22 II. Serum on 2/13/30 Reaction on 2/16/30 Scarlet fever on 2/25/30 III. Serum on 2/14/30 Reaction on 2/20/30 Scarlet fever on 2/27/30

NOTE.—We have received the following comment about serum A from the Connaught Laboratories following our inquiry about our serum reactions. "In looking up what data we have in regard to the same antitoxin used by you, we find that in thirty-seven patients receiving from 15 to 30 cc. as a therapeutic dose, something like 40 per cent showed some evidence of serum sickness. One only of these might be classified as a severe reaction."

DR. G. F. DICK: In reply to Dr. Hess's statistics regarding the recent epidemic at the training school, it is foolish to try to control an epidemic of scarlet fever with antitoxin. Antitoxin control in scarlet fever lasts about a week. You will not get anywhere in attempting to control an epidemic in that way.

DR. JOSEPH CALVIN: As an attack of scarlet fever without treatment with specific antitoxin commonly confers lifetime immunity on the patient, if a therapeutic dose of scarlet fever antitoxin is given early does that patient have a lifetime immunity from scarlet fever, or will he be as liable to have another attack of scarlet fever?

DR. G. F. DICK: It is possible for that person to have another attack, for the earlier the antitoxin is given the less permanent is the immunity obtained. The patient should be tested after the attack and if the Dick test gives positive results he should be actively immunized.

DR. JOSEPH BRENNEMAN: I should like to ask Dr. Dick how definitely he can tell that he has the hemolytic streptococcus of scarlet fever in an ordinary clinical culture. In an article in the German literature recently a man reported a rather large series of cases in which cultures were made from patients with scarlet fever before they left the hospital, and it happened that there were more new contact infections among the patients who had negative hemolytic streptococcus cultures on leaving the hospital, than in those who showed positive reactions.

Another fact that should be thought of in connection with statistics is the fact that scarlet fever has two interesting features. It is not very contagious and the mortality is low, so low that it is hard to compare results and methods of treatment. The mortality in scarlet fever is about from 1 to 2 per cent. A certain amount of this is due to the fact that patients get convalescent serum, a good many are treated in institutions, but so far as I know in the institutions the serum is not used to a great extent and so is not a great factor in lowered mortality. Ten years ago when I was attending physician at St. Vincent's Orphan Asylum, I learned some things about contagion from the good Sister there. She used to say when we had a case of measles, "We will have a lot of measles, but the little ones won't get it." If it was diphtheria she would say, "We will probably have a few scattered cases." If we had a case of scarlet fever she would say, "We won't have a second one," and we rarely did. If it was whooping cough, she would say, "Now we will have a big epidemic and the poor little babies will get it first." In a family of four or five children, if the sick patient with scarlet fever is taken away early, the disease usually does not develop in the rest.

DR. GERALD M. CLINE: Two years ago at the Brokaw Hospital in Bloomington, Ill., an epidemic of scarlet fever started among the nurses. Having had an internship at the Durand Hospital, I got in touch with the Drs. Dick and they were kind enough to send down their co-workers fully equipped. The institution was placed under quarantine, and each nurse showing a positive Dick test was given the prophylactic dose of antitoxin, followed by the scarlet fever toxin. The patients with active cases were treated with the therapeutic dose of antitoxin. Reactions from both were slight. No new cases occurred and quarantine was lifted in about three weeks' time, according to negative cultures from the nose and throat.

At the same time there was a moderate epidemic in the city. I followed the same procedures in my private practice that were used at the hospital, with what I thought to be excellent results and with no serious reactions. I am sorry that I did not bring along a statistical report of this work.

VIOSTEROL: PROPHYLACTIC AND THERAPEUTIC DOSAGE. DR. JULIUS H. HESS, DR. HENRY C. PONCHER, DR. MAURICE L. DALE and REUBEN L. KLEIN.

On Nov. 1, 1928, a clinical investigation with a biologically standardized preparation of viosterol was undertaken. The investigation was started with 225 infants and 162 were retained for the entire period of study. These infants were carefully followed from birth until 1 year of age with monthly roentgen examinations, chemical tests of the blood and physical examinations. The following results were obtained:

Rickets-Prophylactic Studies.—(*a*) In the group given viosterol (sixty-five cases), roentgenographic or blood chemistry evidence of rickets did not develop in any child. In six infants, mild clinical rickets developed. (*b*) In the group given cod liver oil (forty-nine cases), there were roentgenographic and blood chemistry evidence of rickets in two infants and in four others clinical rickets developed. (*c*) In the control cases (forty-six), there was no specific antirachitic therapy. In nine cases marked roentgenographic and blood chemistry evidences of rickets developed and in ten cases clinical rickets developed.

Determination of the Prophylactic Dose.—From the consideration of the observations of our investigations, in no child receiving over 10 drops a day did clinical, roentgenographic or blood chemistry evidence of rickets develop, and 10 drops was the smallest dose that prevented a fall in the serum phosphorus from the first to the later months of life during the infant's first year. We, therefore, consider 10 drops of viosterol daily as the minimum dose for prophylaxis for a normal infant from birth until 1 year. Premature and rapidly growing infants demand separate consideration as to the dosage.

Determination of the Therapeutic Dose.—(*a*) Seventeen cases of rickets showing roentgenographic and blood chemistry changes of varying degree were studied in this phase of the investigation. Six cases of florid rickets were received from outside sources and eleven cases of rickets developed in infants in the control and cod liver oil groups. (*b*) It was not possible to draw conclusions as to the minimum therapeutic dose from the small group of infants that was studied. (*c*) The degree of rickets must be considered in every case. Frequently mild rickets will heal on 10 to 15 drops of viosterol daily, while other cases more advanced will require larger doses. (*d*) Each case of rickets must be given individual consideration. Infants with severe rickets on 30, 40, 50 and 60 drops of viosterol showed uniform healing, clinically, chemically and by x-rays.

The Effect of Massive Doses of Viosterol.—Twelve normal infants were given doses of from 210 to 525 drops of viosterol a day from the second to the fourth week of life to the age of from 6 to 8 months. The following observations were noted: 1. Toxic symptoms were not observed in any of the infants during the period of investigation. 2. There was a definite increase in appetite in practically all of the infants. 3. In the first four months of life (three months on antirachitic therapy) the average weight gain of the infants on massive doses of viosterol fell below that of the children on ordinary doses of viosterol. From the fifth month on, the gain in weight improved, approximating that of the infants on smaller doses. 4. The incidence of diarrhea or vomiting did not differ from similar conditions that were noted at times in the other groups. 5. A comparison of the fontanel areas of the infants in the group receiving from 1 to 20 drops of viosterol daily with the groups of infants on massive doses (from 210 to 525 drops daily) indicates that the large doses hastened the closing of the fontanels to a moderate extent. However, the measurements of the head during the period of observation showed no variation in the various groups. 6. No abnormal serum calcium or phosphorus value was obtained in any of the twelve infants receiving massive doses of viosterol over a period from six to eight months of continuous administration. 7. There was no important change in the hemoglobin and erythrocyte values of these cases.

The Possible Advantages in Feeding Vitamins A and D (Cod Liver Oil) as Against Vitamin D Alone (Viosterol).—This phase of the investigation covered

a period only from birth to 1 year. What effect this difference in feeding would have on subsequent development was not determined in this investigation. No difference was observed in growth (as measured by body length), development of the centers of ossification, age of sitting up, eruption of the first two deciduous teeth, hemoglobin values and red blood cell counts. During the first four months of life the infants on cod liver oil gained better than those on viosterol. However, this ration was not borne out in the general averages after the fourth month. Viosterol in optimum doses was found to be more efficient in maintaining the serum phosphorus level throughout the year.

DISCUSSION

DR. MAURICE L. DALE: I wish to add a few remarks concerning the mode of administration of viosterol. It has been pointed out by Aengenendt, in 1928, and by others since, that when an oily solution of viosterol is given with the food, especially in the bottle, most of it is lost, since it floats to the top when the bottle is inverted and tends to stick to the vessel. In many papers recently reported the results were not commensurate with the dose of viosterol given, and in most cases the fault was in the method of administration. For this reason I adopted the plan, at the start of the experiment, of directing the mothers to give the oil in a teaspoon of orange juice and to watch it float into the child's mouth, thus making sure that all the oil was taken up by the infant.

Another point that I should like to bring out, is the apparent increase in basal metabolism in the infants on excessively high doses of viosterol. This was especially noticeable in the child to whom I was giving 50 mg. of viosterol daily. The symptoms you must all have been impressed by were: a ravenous appetite; a gain in weight not in proportion to the amount of food consumed, and increased activity. This observation has never been mentioned before in the literature except that Hattinger says that the loss in weight was as marked in his animals as though he had fed them thyroid. The symptoms his animals showed, however, aside from the loss in weight, did not suggest an increased basal metabolism, as did the symptoms of our infants.

Book Reviews

Handbuch der Kindertuberkulose. Volume II. Edited by Stefan Engel and Clemens von Pirquet. Price, 149 marks. 170 illustrations, some colored. Leipzig: Georg Thieme, 1930.

The first volume of this exhaustive work on tuberculosis in childhood consisted of 880 pages, and the present volume comprises more than 700. Following a well organized comprehensive plan, the various articles have been written by different authors, and as might have been expected, certain portions of the book far outshadow others. Despite this lack of uniformity and the conflict of opinion which appears from time to time, the main purpose of the editors in thus dividing the responsibility for the handling of an immense amount of material seems to have been accomplished. There is a liveness and vigor to the text which is as refreshing as it is unexpected, and places this work on a high plane of medical literary achievement.

To give some idea of the scope of this volume, under the heading diagnosis is contained chapters on the various types of tuberculin reactions, morphologic blood picture and discussions of complement fixation tests, opsonins, agglutinins and precipitation tests. Next come a chapter on prognosis and one on prophylaxis. Under therapy appear first a discussion of metabolic processes in tuberculosis, then nutritional and tuberculin therapy, with medicinal and physical therapeutic measures, including heliotherapy, sanatorium treatment, etc. The effects of high altitudes and variations in climate in different parts of Europe are discussed not only by German authors, but by French, Dutch, Swiss and others. About fifty pages are given over to a discussion of the orthopedic surgery of tuberculosis, and about twenty-five to the problems of surgical intervention of the chest. Other chapters contain statistical studies, discussions of the influence of age, constitution, development and seeding of peoples. The chapter on incidence, morbidity and autopsy statistics by Alfred Götzl (Vienna), that on orthopedic surgery by Hans Spitzy (Vienna), that on surgical intervention of the lung by Georg Simon and that on tuberculosis in the various phases of childhood by Hans Rietschel (Würzburg) are especially to be commended.

The book is an exceedingly valuable addition to any library and may be strongly recommended to all physicians interested in pediatrics or the study of tuberculosis. Its value, however, would have been considerably enhanced had there been a greater familiarity with the work of American and English or even French investigators. Presumably in an effort to correct this defect, chapters have been included by several French authors, as well as one by Dr. Isaac Abt of Chicago and another by Dr. Bela Schick of New York.

The paper, print and illustrations are excellent, as is the case with most German texts, and there is an extensive bibliography, deficient only in the lack of foreign references.

Diseases of the Urinary Tract in Children. By Edwin Beer, M.D., and Abraham Hyman, M.D. Price, $6. Pp. 318, with 50 illustrations. New York: Paul B. Hoeber, Inc., 1930.

This book, written in monographic form, is based on rather extensive experience mostly in the wards of Mount Sinai Hospital, New York. It is an excellent example of hospital cooperation between the departments of pediatrics and urology and shows what the fruits of this type of cooperation may be.

Each chapter is presented in the form of an essay, hence the sequence which is the method of the usual textbook is lacking.

General symptoms and the various methods of examination are briefly but clearly presented. The chapters on enuresis, infections of the urinary tract, abscess

and carbuncle of the kidney, foreign bodies in the urinary tract, congenital anomalies of the upper urinary tract, urinary lithiasis, chronic renal tuberculosis, injuries and tumors leave nothing to be desired in the matter of thoroughness.

Attention should be called to the chapter on pyelitis, because not only is it well written, but it presents in a concise form the views as they are known today. Malignant tumors of the kidneys, always an interesting subject, are discussed from the various angles that make for enlightenment, and the different theories of the origin of tumors of the kidneys in children are not neglected.

To the pediatrician especially and also to the general practitioner the chapter dealing with disturbances in the outflow of urine from the bladder as well as obstruction at the neck of the bladder and in the urethra and diverticulum of the bladder, should be of great interest. These complications are of undeniable importance because of their damaging effects in the higher urinary tract. The fact that hitherto they have received but scant attention in the literature adds to the value of the book under consideration.

This book, dealing as it does with diagnosis, pathology and treatment, should prove of exceeding value to the general practitioner who, as a rule, sees these cases first, to the pediatrician whose training generally lacks a urologic point of view and to the urologist whose work has been wholly or almost wholly confined to the adult.

The book is profusely illustrated, and each chapter contains an excellent bibliography that is of particular value to those interested in the subject.

LES VOMISSEMENTS CHEZ LE NOURRISSON. By E. LESNÉ and M. COFFIN. Price, 25 francs. Pp. 140, with 21 figures and photographs. Paris: Gauthier-Villars & Cie, 1930.

The first two chapters of this book consider the character and causes of vomiting in the infant. The pathology, classification, gastric content and roentgenologic aspects and the various causes of vomiting are discussed. The last two chapters are devoted to pylorospasm and pyloric stenosis. The book is well written, the subject matter being taken from cases in the author's experience. A review of the literature is well discussed.

LES CURES THERMALES ET CLIMATIQUES CHEZ LES ENFANTS. By M. VILLARET and F. SAINT-GIRONS. Price, 10 francs. Pp. 128. Paris: L'Expansion Scientifique Française, 1930.

Like the other volumes of this series, the book is well written and compact. The first part deals with conditions in children that are benefited by mineral springs, fresh air, high altitude, sea air, or water and heliotherapy and physical education. The final part of the book contains a brief sketch of all of the well known health resorts for children in France.

Directory of Pediatric Societies

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Philadelphia. Time: 1931.

American Academy of Pediatrics

President: Dr. I. A. Abt, 104 S. Michigan Ave., Chicago.
Secretary: Dr. C. G. Grulee, 310 S. Michigan Ave., Chicago.

American Child Health Association

President: Hon. Herbert Hoover, 370 7th Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 7th Ave., New York.

American Pediatric Society

President: Dr. Philip Van Ingen, 125 E. 71st St., New York.
Secretary-Treasurer. Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.

Association of American Teachers of the Diseases of Children

President: Jacob V. Greenebaum, 19 W. 8th St., Cincinnati.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Philadelphia. Time: 1931.

Children's Hospital Association of America

President: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary-Treasurer: Miss Bena M. Henderson, Milwaukee Children's Hospital, Milwaukee.
Place: New Orleans, La. Time: October, 1930.

Canadian Society for the Study of Diseases of Children

President: Dr. E. A. Morgan, 160 Bloor St., Toronto, Ont.
Secretary-Treasurer: Dr. George E. Smith, 244 Bloor St., W., Toronto, Ont.

SECTIONAL

Central States Pediatric Society

President: Dr. Edward Clay Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Blvd., Chicago.
Place: Memphis, Tenn. Time: Fall, 1930.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. H. Leslie Moore, 1717 Pacific Ave., Dallas, Texas.
Secretary: Dr. Ludo von Meysenbug, 3501 Prytania St., New Orleans, La.
Place: Louisville, Ky.: November, 1930.

STATE

Alabama Pediatric Society

President: Dr. Hughes Kennedy, Jr., Highland Plaza Apts., Birmingham.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22nd St., Birmingham.

Georgia Pediatric Society

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary-Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

Louisiana State Pediatric Society

President: Dr. R. A. Strong, 1551 Canal St., New Orleans.
Secretary-Treasurer: Dr. Suzanne Schaeffer, Chailie Bldg., New Orleans.

Oklahoma State Pediatric Society

President: Dr. Carroll M. Pounders, 210 W. 10th St., Oklahoma City.
Secretary: Dr. C. E. Bradey, Medical Arts Bldg., Tulsa.
Place: Oklahoma City. Time: May, 1931.

South Carolina Pediatric Society

President: Dr. M. W. Beach, 126 Meeting St., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, The McLeod Infirmary, Florence.

Texas Pediatric Society

President: Dr. L. O. Godley, Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. P. E. Luecke, 4105 Live Oak St., Dallas.

Virginia Pediatric Society

President: Dr. Franklin D. Wilson, 136 York St., Norfolk.
Secretary: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. John Toomey, Cleveland City Hospital, Cleveland.
Secretary: Dr. A. B. Grossman, 7016 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., West, Toronto.
Time: November 17, December 15, February 16 and March 15.

Bronx Pediatric Society

President: Dr. David I. Frey, 2065 Grand Concourse, New York.
Secretary: Dr. H. M. Eisenoff, 1018 E. 163rd St., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Secretary: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Arthur H. Parmelee, 310 S. Michigan Blvd., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Detroit Pediatric Society

President: Dr. Wyman C. C. Cole, 2970 W. Grand Blvd., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Perry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. G. J. Levy, 899 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. M. G. Peterman, 167 17th St., Milwaukee.
Secretary: Dr. F. R. Janney, 418 E. North Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

Nebraska Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

New England Pediatric Society

President: Dr. Grover F. Powers, New Haven, Conn.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: October, January and March.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Hugh Chaplin, 39 E. 75th St., New York.
Secretary: Dr. John P. Caffey, Babies' Hospital, 167th Street and Broadway, New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

North Pacific Pediatric Society

President: Dr. Eber D. Kanaga, Townsend Bldg., Tacoma, Wash.
Secretary: Dr. Homer T. Clay, Washington Bldg., Tacoma, Wash.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Secretary: Dr. F. G. Hedenstrom, 218 Lowry Bldg., St. Paul.
Place: University Campus and Rochester, Minn. Time: Winter, Spring, Summer, Fall.

Philadelphia Pediatric Society

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. Basil B. Jones, 2618 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Howard F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. Bernard C. Dorset, 1612 Tremont St., Denver.
Secretary-Treasurer: Dr. Wilford W. Barber, 227, 16th St., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Gustave Lippmann, 3720 Washington Blvd., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, 3720 Washington Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

Seattle Pediatric Society

President: Dr. Vernon W. Spickard, Cobb Bldg., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. William S. Bowers, 1136 W. 6th St., Los Angeles.
Secretary: Dr. Fred L. Glascock, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. W. D. Lyon, 101 S. Balch St., Akron, Ohio.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November 14 and 15, 1930.